'A very good overview of what one needs to know when working with people infected with HIV.' Dr. Beth Harley, *Southern African Journal of HIV Medicine*

Adult HIV

What health professionals need to know

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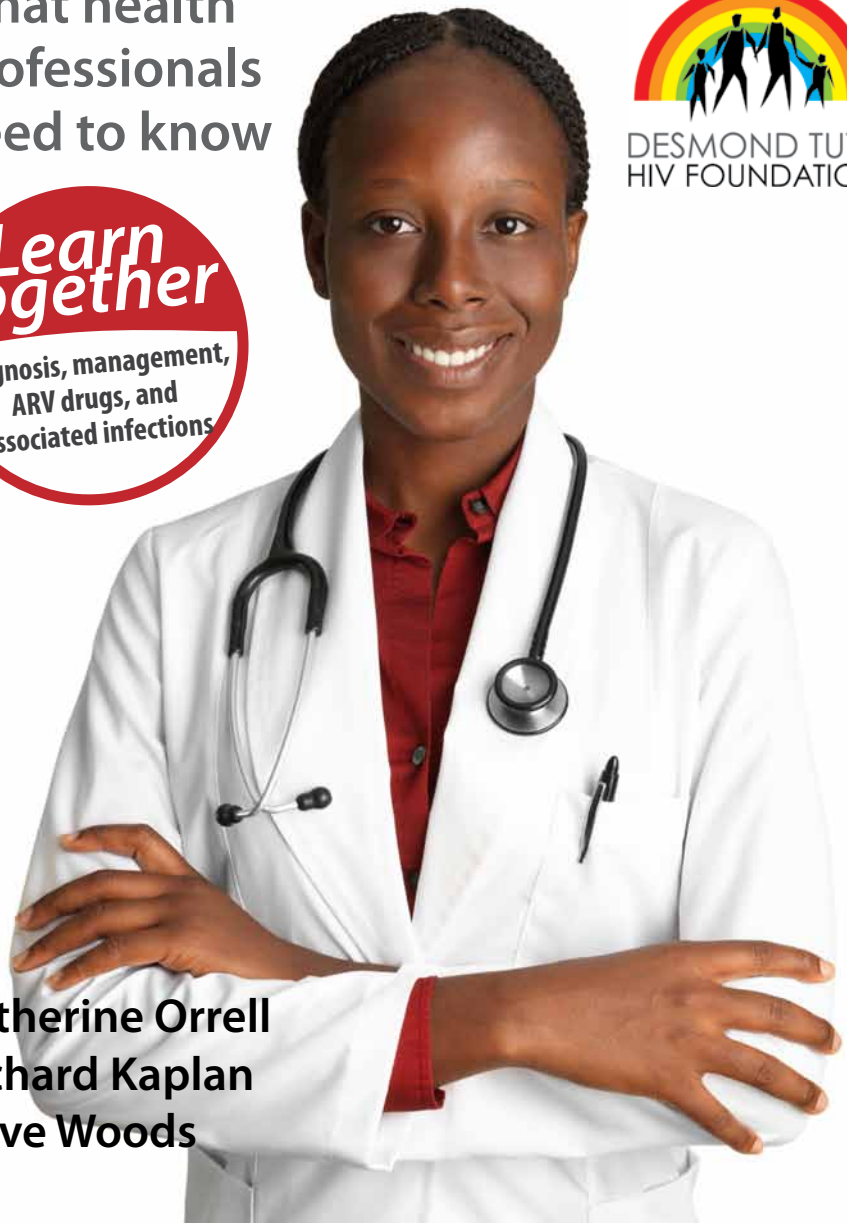

Catherine Orrell
Richard Kaplan
Dave Woods

Adult HIV

What health professionals need to know

Developed by the Desmond Tutu HIV Foundation as part of the Adult HIV Education Programme

bettercare
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Editors: Dr C. Orrell, Dr R. Kaplan, Prof D. Woods

Editorial Board: Prof L-G. Bekker, Ms F. Cope, Ms K. Fosseus, Dr C. Orrell, Ms L. Mtwisha, Dr R. Kaplan, Prof D. Woods

Contributors: Dr M. Blockman, Dr K. Dong, Dr C. Horwood, Prof D. Martin, Dr D. Wilson, Dr F. Venter, Prof R. Wood, Dr B. Harley

Disclaimer

We have taken every care to ensure that drug dosages and related medical advice in this book are accurate. However, drug dosages can change and are updated often, so always double-check dosages and procedures against a reliable, up-to-date formulary and the given drug's documentation before administering it.

Adult HIV: What health professionals need to know

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Comments and suggestions by all the participants who use Adult HIV to further their own continuing education will provide ongoing feedback.

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Prof Dave Woods
Editor

Introduction

About the Bettercare series

Bettercare publishes an innovative series of distance-learning books for healthcare professionals, developed by the Perinatal Education Trust, Eduhealthcare, the Desmond Tutu HIV Foundation and the Desmond Tutu TB Centre, with contributions from numerous experts.

Our aim is to provide appropriate, affordable and up-to-date learning material for healthcare workers in under-resourced areas, so that they can manage their own continuing education courses which will enable them to learn, practise and deliver skillful, efficient patient care.

The Bettercare series is built on the experience of the Perinatal Education Programme (PEP), which has provided learning opportunities to over 60 000 nurses and doctors in South Africa since 1992. Many of the educational methods developed by PEP are now being adopted by the World Health Organisation (WHO).

Why decentralised learning?

Continuing education for healthcare workers traditionally consists of courses and workshops run by formal trainers at large central hospitals. These teaching courses are expensive to attend, often far away from the healthcare workers' families and places of work, and the content frequently fails to address the real healthcare requirements of the poor, rural communities who face the biggest healthcare challenges.

To help solve these many problems, a self-help decentralised learning method has been developed which addresses the needs of professional healthcare workers, especially those in poor, rural communities.

Books in the Bettercare series

Maternal Care addresses all the common and important problems that occur during pregnancy, labour, delivery and the puerperium. It covers the antenatal and postnatal care of healthy women with normal pregnancies, monitoring and managing the progress of labour, specific medical problems during pregnancy, labour

and the puerperium, family planning and regionalised perinatal care. Skills workshops teach clinical examination in pregnancy and labour, routine screening tests, the use of an antenatal card and partogram, measuring blood pressure, detecting proteinuria and performing and repairing an episiotomy.

Maternal Care is aimed at healthcare workers in level 1 hospitals or clinics.

Primary Maternal Care addresses the needs of healthcare workers who provide antenatal and postnatal care, but do not conduct deliveries. It is adapted from theory chapters and skills workshops from *Maternal Care*. This book is ideal for midwives and doctors providing primary maternal care in level 1 district hospitals and clinics, and complements the national protocol of antenatal care in South Africa.

Intrapartum Care was developed for doctors and advanced midwives who care for women who deliver in district hospitals. It contains theory chapters and skills workshops adapted from the labour chapters of *Maternal Care*. Particular attention is given to the care of the mother, the management of labour and monitoring the wellbeing of the fetus. *Intrapartum Care* was written to support and complement the national protocol of intrapartum care in South Africa.

Newborn Care was written for healthcare workers providing special care for newborn infants in regional hospitals. It covers resuscitation at birth, assessing infant size and gestational age, routine care and feeding of both normal and high-risk infants, the prevention, diagnosis and management of hypothermia, hypoglycaemia, jaundice, respiratory distress, infection, trauma, bleeding and congenital abnormalities, as well as communication with parents. Skills workshops address resuscitation, size measurement, history, examination and clinical notes, nasogastric feeds, intravenous infusions, use of incubators, measuring blood glucose concentration, insertion of an umbilical vein catheter, phototherapy, apnoea monitors and oxygen therapy.

Primary Newborn Care was written specifically for nurses and doctors who provide primary care for newborn infants in level 1 clinics and hospitals. *Primary Newborn Care* addresses the care of infants at birth, care of normal infants, care of low-birth-weight infants, neonatal emergencies, and common minor problems in newborn infants.

Mother and Baby Friendly Care describes gentler, kinder, evidence-based ways of caring for women during pregnancy, labour and delivery. It also presents improved methods of providing infant care with an emphasis on kangaroo mother care and exclusive breastfeeding.

Saving Mothers and Babies was developed in response to the high maternal and perinatal mortality rates found in most developing countries. Learning material used in this book is based on the results of the annual confidential enquiries into maternal deaths and the Saving Mothers and Saving Babies reports published in South Africa. It addresses the basic

principles of mortality audit, maternal mortality, perinatal mortality, managing mortality meetings and ways of reducing maternal and perinatal mortality rates. This book should be used together with the Perinatal Problem Identification Programme (PPIP).

Birth Defects was written for healthcare workers who look after individuals with birth defects, their families, and women who are at increased risk of giving birth to an infant with a birth defect. Special attention is given to modes of inheritance, medical genetic counselling, and birth defects due to chromosomal abnormalities, single gene defects, teratogens and multifactorial inheritance. This book is being used in the Genetics Education Programme which trains healthcare workers in genetic counselling in South Africa.

Perinatal HIV enables midwives, nurses and doctors to care for pregnant women and their infants in communities where HIV infection is common. Special emphasis has been placed on the prevention of mother-to-infant transmission of HIV. It covers the basics of HIV infection and screening, antenatal and intrapartum care of women with HIV infection, care of HIV-exposed newborn infants, and parent counselling.

Childhood HIV enables nurses and doctors to care for children with HIV infection. It addresses an introduction to HIV in children, the clinical and immunological diagnosis of HIV infection, management of children with and without antiretroviral treatment, antiretroviral drugs, opportunistic infections and end-of-life care.

Childhood TB was written to enable healthcare workers to learn about the primary care of children with tuberculosis. The book covers an introduction to TB infection, and the clinical presentation, diagnosis, management and prevention of tuberculosis in children and HIV/TB co-infection. *Childhood TB* was developed by paediatricians with wide experience in the care of children with tuberculosis, under the auspices of the Desmond Tutu Tuberculosis Centre at the University of Stellenbosch.

Child Healthcare addresses all the common and important clinical problems in children, including immunisation, history and examination, growth and nutrition, acute and chronic infections, parasites, skin conditions, and difficulties in the home and society. *Child Healthcare* was developed for use in primary care settings.

Adult HIV covers an introduction to HIV infection, management of HIV-infected adults at primary-care clinics, preparing patients for antiretroviral (ARV) treatment, ARV drugs, starting and maintaining patients on ARV treatment and an approach to opportunistic infections. *Adult HIV* was developed by doctors and nurses with wide experience in the care of adults with HIV, under the auspices of the Desmond Tutu HIV Foundation at the University of Cape Town.

Well Women was written for primary health workers who manage the everyday health needs of women. It

covers reproductive health, family planning and infertility, common genital infections, vaginal bleeding, and the abuse of women.

Breast Care was written for nurses and doctors who manage the health needs of women from childhood to old age. It covers the assessment and management of benign breast conditions, breast cancer and palliative care.

Infection Prevention and Control was written for nurses, doctors, and health administrators working in the field of infection prevention and control, particularly in resource-limited settings. It includes chapters on IPC programmes, risk management, health facility design, outbreak surveillance and antimicrobial stewardship.

Format of the courses

1. Objectives

The learning objectives are clearly stated at the start of each chapter. They help the participant to identify and understand the important lessons to be learned.

2. Pre- and post-tests

There is a multiple-choice test of 20 questions for each chapter at the end of the book. Participants are encouraged to take a pre-test before starting each chapter, to benchmark their current knowledge, and a post-test after each chapter, to assess what they have learned.

Self-assessment allows participants to monitor their own progress through the course.

3. Question-and-answer format

Theoretical knowledge is presented in a question-and-answer format, which encourages the learner to actively participate in the learning process. In this way, the participant is led step by step through the definitions, causes, diagnosis, prevention, dangers and management of a particular problem.

Participants should cover the answer for a few minutes with a piece of paper while thinking about the correct reply to each question. This method helps learning.

Simplified flow diagrams are also used, where necessary, to indicate the correct approach to diagnosing or managing a particular problem.

Each question is written in bold, like this, and is identified with the number of the chapter, followed by the number of the question, e.g. 5-23.

4. Important lessons

Important practical lessons are emphasised like this.

5. Notes

NOTE Additional, non-essential information is provided for interest and given in notes like this. These facts are not used in the case studies or included in the multiple-choice questions.

6. Case studies

Each chapter closes with a few case studies which encourage the

participant to consolidate and apply what was learned earlier in the chapter. These studies give the participant an opportunity to see the problem as it usually presents itself in the clinic or hospital. The participant should attempt to answer each question in the case study before reading the correct answer.

7. Practical training

Certain chapters contain skills workshops, which need to be practised by the participants (preferably in groups). The skills workshops, which are often illustrated with line drawings, list essential equipment and present step-by-step instructions on how to perform each task. If participants aren't familiar with a practical skill, they are encouraged to ask an appropriate medical or nursing colleague to demonstrate the clinical skill to them. In this way, senior personnel are encouraged to share their skills with their colleagues.

8. Final examination

On completion of this course, participants can take a 75-question multiple-choice examination.

All the exam questions will be taken from the multiple-choice tests from the book. The content of the skills workshops will not be included in the examination.

Participants need to achieve at least 80% in the examination in order to successfully complete the course. Successful candidates will be sent a certificate which states that they have successfully completed that course. Bettercare courses are not yet accredited for nurses, but South African doctors can earn CPD points on the successful completion of an examination.

Please contact the Perinatal Education Programme when you are eady to take the exam.

Contributors

The developers of our learning materials are a multi-disciplinary team of nurses, midwives, obstetricians, neonatologists, and general paediatricians. The development and review of all course material is overseen by the Editor-in-Chief, emeritus Professor Dave Woods, a previous head of neonatal medicine at the University of Cape Town who now consults to UNICEF and the WHO.

Perinatal Education Trust

Books developed by the Perinatal Education Programme are provided as cheaply as possible. Writing and updating the programme is both funded and managed on a non-profit basis by the Perinatal Education Trust.

Eduhealthcare

Eduhealthcare is a non-profit organisation based in South Africa. It aims to improve health and wellbeing, especially in poor communities, through affordable education for healthcare workers. To this end it provides financial support for the development and publishing of the Bettercare series.

The Desmond Tutu HIV Foundation

The Desmond Tutu HIV Foundation at the University of Cape Town, South Africa, is a centre of excellence in HIV medicine, building capacity through training and enhancing knowledge through research.

The Desmond Tutu Tuberculosis Centre

The Desmond Tutu Tuberculosis Centre at Stellenbosch University, South Africa, strives to improve the health of vulnerable groups through the education of healthcare workers and community members, and by influencing policy based on research into the epidemiology of childhood tuberculosis, multi-drug-resistant tuberculosis, HIV/TB co-infection and preventing the spread of TB and HIV in southern Africa.

Updating the course material

Bettercare learning materials are regularly updated to keep up with developments and changes in healthcare protocols. Course participants can make important contributions to the continual improvement of Bettercare books by reporting factual or language errors, by identifying sections that are difficult to understand, and by suggesting additions or improvements to the contents. Details of alternative or better forms of management would be particularly appreciated. Please send any comments or suggestions to the Editor-in-Chief, Professor Dave Woods.

Contact information

Bettercare

Website: www.bettercare.co.za
Email: info@bettercare.co.za
Cell: 076 657 0353
Fax: 086 219 8093
Post: 3rd Floor, Sunclare Building, 21 Dreyer Street, Claremont, 7708

Eduhealthcare

Director: Professor Dave Woods
Website: www.pepcourse.co.za
Email: pepcourse@mweb.co.za
Phone/fax: 021 786 5369
Post: Eduhealthcare,
70 Dorries Drive, Simon's Town, 7975

Desmond Tutu HIV Foundation

Website:
www.desmondtutuhivfoundation.org.za
Email: adulthiv@hiv-research.org.za
Tel: 021 650 6966
Fax: 021 650 6963
Post: Desmond Tutu HIV Foundation
Level One, Wernher Beit North Building, Faculty of Health Sciences
Anzio Road, Observatory, 7925, Cape Town

1

HIV infection

Before you begin this unit, please take the corresponding test to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- Define HIV infection and AIDS.
- Explain how HIV is transmitted between people.
- Appreciate why HIV infection is having a devastating effect on society.
- Confirm the clinical diagnosis of HIV infection.
- Describe acute seroconversion illness.
- Explain the asymptomatic and symptomatic phases of HIV infection.
- Describe the 4 clinical stages of HIV infection.
- Recognise the clinical signs of HIV infection.

Introduction to HIV infection

1-1 What is HIV?

HIV, the human immunodeficiency virus, is a virus which infects people for life.

Viruses are extremely small, very simple organisms which can only exist and multiply by invading and taking control of a plant or animal cell (the host cell). Viruses are responsible for many diseases such as influenza and the common cold. Unlike bacteria they are not killed by antibiotics. Viruses may be divided into many different groups. HIV belongs to a group of viruses known as retroviruses.

People infected with HIV are said to be HIV positive.

HIV is the human immunodeficiency virus.

NOTE HIV was first identified in 1983 by a research group headed by Luc Montagnier working in the Pasteur Institute in Paris. HIV is a new human virus which probably first appeared in the 1950s when it was transmitted to humans from chimpanzees in central Africa.

1-2 What are retroviruses?

They are a group of viruses which are unique in nature as they have a special enzyme called reverse transcriptase. This enzyme enables HIV to introduce its own genes into the nucleus of the host cell. The host cell is then instructed to produce millions of new copies of the virus. These are released into the bloodstream and can then infect other cells. Retroviruses usually cause long periods of silent infection before signs of disease appear.

NOTE Retroviruses contain an RNA genetic code. The enzyme reverse transcriptase allows HIV to make double-strand DNA copies of its single-strand RNA. The DNA copy is then inserted into the DNA of the nucleus in the host cell. Only retroviruses have this ability to make a DNA copy of their RNA code. Retroviruses are common and some cause cancers in animals.

HIV is a retrovirus.

1-3 What disease is caused by HIV?

HIV causes AIDS (Acquired Immunodeficiency Syndrome). Without treatment with antiretroviral drugs, AIDS is a fatal condition.

HIV causes AIDS.

1-4 What is AIDS?

AIDS is a clinical syndrome which presents in people with advanced HIV infection (severe HIV disease). It can present in many different ways. The symptoms and signs of AIDS are usually due to secondary infections with a number of different organisms not normally seen in HIV-negative people. People with AIDS are always HIV positive.

The terms 'symptomatic HIV' or 'HIV disease' are also used for patients who are clinically ill because of HIV. These patients may not yet be ill enough to be labelled as having AIDS.

AIDS is a severe illness which presents in people who have advanced HIV infection.

1-5 How does HIV cause disease?

HIV invades and destroys the immune system by damaging the CD4 lymphocytes. As the CD4 cells play a very important role in the functioning of the immune system, HIV infection of CD4 cells damages the immune system, leading to immune deficiency. Therefore, HIV destroys more and more CD4 cells, and the body's immune system becomes weaker and weaker.

The normal immune system protects the body against infection. Therefore, by killing CD4 cells, HIV weakens the immune system which is then no longer able to prevent infection by many viruses, bacteria, fungi and parasites.

HIV infection damages the immune system.

NOTE About 10 billion copies of HIV are produced each day in infected people.

1-6 Are there different types of HIV?

Two types of HIV are recognised, HIV1 and HIV2. Most HIV infection in southern Africa is caused by HIV1, which has many subtypes (clades). The important subtype in Africa is subtype C. Subtype B is the most common subtype in the developed world.

The spread of HIV

1-7 Is HIV infectious?

Yes. HIV infection can be spread from one person to another.

1-8 How is HIV transmitted from one person to another?

The virus may be transmitted from one person to another by:

1. Unprotected sexual contact (horizontal transmission). Body fluids such as vaginal and cervical secretions, semen and blood contain large amounts of HIV. HIV is not present in urine or stool, while very little is present in saliva.
2. Crossing from a mother to her fetus or newborn infant (vertical transmission).
3. Using syringes, needles or blades which are soiled with HIV-infected blood. They may be shared by intravenous drug abusers or not correctly cleaned and then reused by health workers.
4. Accidental needle-stick injuries.
5. A blood transfusion with HIV-infected blood or other HIV-infected blood products such as factor VIII in haemophiliacs. This is very rare in South Africa, where all blood products are screened for HIV.

There is no evidence that HIV can be spread by mosquitoes, lice or bed bugs. In Africa, HIV is most commonly spread by heterosexual intercourse.

1-9 What forms of sexual contact may transmit HIV?

HIV is almost always transmitted by penetrative sexual intercourse (heterosexual or homosexual). However, all forms of oral sexual contact (mouth to vagina or mouth to penis) can also result in infection, although the risk is less. Deep kissing rarely transmits HIV, unless mouth ulcers are present. HIV cannot penetrate intact skin but may infect through open sores, cuts and abrasions, or mucous membranes. Circumcision offers some protection against acquiring HIV infection, i.e. infection is more common in uncircumcised men than circumcised men. The highest risk of sexual transmission for both men and women is during anal intercourse. The thin, friable rectal mucosa is easily damaged during anal intercourse, which increases the risk of infection. The presence of any other sexually transmitted infection will also increase the risk of HIV infection.

In South Africa, HIV is usually spread by sexual intercourse.

Sexual abuse and rape may also result in HIV infection.

1-10 Can you become infected with HIV during normal social contact?

No. Family and friends of an HIV-infected person do not become infected except by sexual contact. HIV is not transmitted by close social contact such as touching, holding hands, hugging and social kissing. HIV is also not spread by coughing, sneezing, swimming pools, toilet seats, sharing cooking, drinking and eating utensils or by changing a nappy. However, any bleeding, such as nose bleeds, may spread HIV.

1-11 How can the sexual spread of HIV in the general public be reduced?

Through the behavioural change of 'ABC':

1. 'A' – Abstinence (no sex) and delay in sexual debut (first-time sex).
2. 'B' – Be faithful to one partner (reduce the number of sexual partners).
3. 'C' – Use a condom (especially when not being faithful to one partner).

The reduction in number of sexual partners seems to have resulted in the declining HIV prevalence in some countries. However, all three behavioural changes are important.

1-12 Can you have HIV infection and not be ill?

Yes. A person is usually infected with HIV for years before becoming ill. Therefore, most people infected with HIV are clinically well (asymptomatic) for many years.

1-13 Can an HIV-infected person who is well transmit the virus?

Yes. HIV is frequently transmitted by people who appear to be clinically well but are infected with HIV. This is the great danger of HIV infection as most infected people do not know that they have been infected. They are also unaware that they may transmit HIV to another person.

1-14 How common is HIV infection?

Over 35 million people worldwide have HIV infection. It was estimated that 6.4 million South Africans were living with HIV in 2012. In 2011, 29.5% of all pregnant women in South Africa were infected with HIV. The province of KwaZulu–Natal had the highest prevalence of 37.4%. In some antenatal clinics, more than 50% of pregnant women were HIV positive.

1-15 How often does HIV infection cause death?

It is estimated that over 600 people die of HIV infection each day in South Africa. Many of these deaths could be prevented with the correct treatment. Without antiretroviral treatment most people with HIV infection will eventually die of AIDS.

1-16 Is the HIV epidemic in South Africa still expanding?

No. The rate of HIV infection in women attending state antenatal care clinics in South Africa has been stable at around 29% from 2007 to 2011. But this is very high and though HIV infections have decreased, in South Africa over one

thousand people are still infected with HIV every day.

South Africa has one of the largest HIV epidemics in the world.

1-17 What is the risk of HIV crossing from an infected mother to her infant?

The risk of HIV crossing the placenta during pregnancy is 5%, while the risk of HIV infecting the infant during labour and vaginal delivery is 15%. Without HIV prophylaxis with antiretroviral drugs the overall risk during pregnancy, labour and vaginal delivery is therefore 20%.

There is an additional risk of 15% if the mother practises mixed breastfeeding (breast milk plus other liquids and solids) for two years. The total risk of mother-to-child transmission (MTCT) in these breastfed infants is therefore 35%. The risk of breast milk transmission is 5% for the first six months, 5% for the second six months and 5% for the second year. With exclusive breastfeeding (breast milk only) for six months, the risk is much lower.

1-18 How can the risk of mother-to-child infection be reduced?

The most effective method in women with HIV infection is to use antiretroviral drugs prophylactically. The risk of mother-to-child transmission can be reduced to below 2% by:

1. Giving all HIV-positive pregnant women antiretroviral therapy (ART) from their first antenatal visit to be continued indefinitely or until the end of breast feeding.The ART consists of triple therapy for the mother during pregnancy and breast feeding and nevirapine for the child during breast feeding.
2. Giving daily nevirapine to the infant for six weeks after birth and then continuing for as long as there is any breastfeeding.

With the roll-out of the prevention of mother-to-child transmission (PMTCT) programme, the number of HIV-infected children should be greatly reduced.

The use of prophylactic antiretroviral drugs reduces the risk of mother-to-child transmission.

1-19 What is the impact of HIV infection on society?

The epidemic of HIV infection has had devastating impact on society in South Africa and other countries in sub-Saharan Africa. At the peak of the AIDS epidemic in South Africa, the average life expectancy fell to around 45 years but has increased to around 60 years following the roll out of ART.

In Africa, most people with HIV infection are female and most are from poor communities. This has a massive effect on families and increases the risk of childhood under-nutrition and death, even in HIV-negative children.

As a result of the number of deaths, ill people and homeless children, HIV infection has had an enormous social and financial impact on all communities, and has placed a strain on the health services.

Every effort must be made to prevent women becoming infected with HIV. This is the most effective way of preventing HIV infection in children.

NOTE: A combination of preventative methods is most effective, e.g. circumcision and regular condom use. Pre-exposure prophylaxis in an HIV negative woman or ART in HIV discordant couples, where only one partner is HIV positive, has been successful when added to other preventative methods.

Screening for HIV infection

1-20 How is the clinical suspicion of HIV infection confirmed?

By either detecting antibodies to the virus or identifying part of the virus in the blood.

1-21 Should people be counselled before HIV testing?

People must be informed and counselled before blood tests are done to confirm or exclude HIV infection. It should be documented that the person consents to screening. It is considered unethical practice to perform HIV screening tests without the person's permission. HIV screening is very important as it is the 'gateway to care'.

1-22 What tests are available to screen for HIV infection?

A number of tests are available to screen people for HIV infection:

1. Rapid test
2. ELISA (Enzyme-Linked Immunosorbent Assay) test
3. PCR (Polymerase Chain Reaction) test
4. P24 antigen test

See skills workshop 6A for how to do a rapid test.

NOTE HIV culture and testing for other HIV antigens can also be done. These are expensive tests and are only used in research or in cases where the diagnosis of HIV infection is difficult. The Western blot test is the most accurate test for detecting virus antibodies, and is used in the laboratory to make a diagnosis in difficult cases with conflicting results with the ELISA or rapid test.

1-23 What are the rapid and ELISA screening tests?

These are commonly used blood tests to screen well people for HIV infection and also to confirm HIV infection in people who have symptoms and signs. Both are cheap and very accurate, and become positive if antibodies to HIV are present. These tests do not determine whether the actual virus is present, but rather the body's response to the HIV infection. Therefore, they are highly reliable but indirect tests for HIV. The rapid test is most commonly used to screen for HIV infection.

The rapid test is the most common method used to screen people for HIV infection.

NOTE Both ELISA and rapid tests are 99% accurate if performed correctly and are confirmed with a second test using a kit from another manufacturer.

1-24 How is the ELISA test done?

The ELISA test is done by a laboratory on a sample of venous blood taken from the person. 1 to 2 ml of clotted blood is needed. The laboratory should provide a result within 24 hours. The result is either positive or negative. The disadvantage of the ELISA test is that it cannot be done at a clinic.

1-25 How is the rapid test done?

The great advantage of the rapid test is that it can be done on a drop of blood in a clinic and blood does not have to be sent to a laboratory. There are a number of manufacturers who provide rapid tests. They are very similar, but not exactly the same. If a rapid test is positive with one kit, it is important to repeat the test with another kit from a different manufacturer to confirm that the person really is HIV positive.

1. If the first rapid test is negative, accept that the person is HIV negative.
2. If two rapid tests on different kits are positive, accept that the person is HIV positive.
3. If the first test is positive and the second is negative, send blood to the laboratory for an ELISA test to decide whether the person is HIV positive or negative.

In order to detect false-positive tests (the test is positive but the patient is not infected with HIV), all positive screening tests should be repeated with another kit or with another type of test.

1-26 What is the PCR test?

This test determines whether there is DNA from the HIV (genetic material from the nucleus of the virus) present in the lymphocytes in the person's blood. The PCR test is very useful in screening infants younger than 18 months for HIV infection as the rapid and ELISA tests are unreliable to confirm HIV infection at this time, due to the possible presence of maternal antibodies.

NOTE The HIV DNA PCR test (qualitative) detects the presence of the virus within cells while the HIV RNA PCR test (quantitative) measures the amount of virus in the blood (viral load). The latter test may not be reliable to screen for HIV infection.

The PCR test detects very small amounts of HIV material in the blood.

1-27 What is the p24 antigen test?

P24 antigen is part of the virus. The p24 antigen test detects this HIV material in the blood. The ultrasensitive p24 antigen test is very accurate.

1-28 When do these tests become positive if a person is infected with HIV?

They may become positive as early as two weeks after infection, but most are reliable from six weeks after infection.

1-29 What is the window period?

This is the period of time between infection and the test becoming positive. During this time the test may give a false-negative result (the patient is infected with HIV but the test is still negative). For most tests, the window period lasts up to six weeks. Rarely, the window period may be longer, up to three months. With new, highly sensitive tests the window period is shortening.

1-30 What is the CD4 count?

CD4 cells are lymphocytes that play a very important role in the normal functioning of the immune system. HIV attaches to CD4 cells and kills them. As a result, the number of CD4 cells gradually falls as the HIV infection progresses, and more and more CD4 cells are killed. Therefore the CD4 count is the best measure of the degree that HIV has damaged the immune system. The normal CD4 count in a healthy adult is above 500 cells/μl.

The CD4 count measures the degree of damage done by HIV to the immune system.

NOTE A low CD4 count must not be used to diagnose HIV infection as there are other causes of reduced CD4 cells.

1-31 What is the viral load?

The viral load is a measure of the amount of HIV in the blood. The higher the viral load, the faster the HIV is multiplying. A high viral load indicates that there is a lot of HIV in the blood (and other body secretions). Viral load is usually expressed as RNA copies/ml.

The viral load is a measure of the amount of HIV in the blood.

Clinical presentation of HIV infection

1-32 What are the three phases of HIV infection?

HIV infection can be divided into three phases.

1. Acute seroconversion illness (which only occurs in 50% of people)
2. The latent, silent, asymptomatic phase
3. The chronic disease when HIV infection becomes symptomatic

1-33 What is acute seroconversion illness?

In response to infection with HIV, the immune system produces antibodies against the virus. Unfortunately these antibodies fail to kill all the HIV. At the time that HIV antibodies appear in the blood (seroconversion) about 50% of people develop a flu-like illness which lasts a few days or weeks. Acute seroconversion illness presents two to six weeks after infection with HIV.

During acute seroconversion illness the viral load is very high and the CD4 count may be temporarily depressed. The screening tests for HIV may still be negative at the time of acute seroconversion illness, and only becomes positive a few weeks later.

Infection with HIV may cause acute seroconversion illness.

NOTE Patients who develop severe acute seroconversion illness usually progress to AIDS faster than those who are asymptomatic while seroconverting. They should be closely followed up.

1-34 What are the common features of acute seroconversion illness?

The common features of acute seroconversion illness are:

1. Fever
2. General tiredness
3. Headache
4. Cough or sore throat
5. Muscle or joint pains
6. Nausea, vomiting or diarrhoea
7. Enlarged lymph nodes (lymphadenopathy)
8. A measles-like rash
9. Oral or genital ulcers

The above signs and symptoms are similar to those found in glandular fever (infectious mononucleosis).

NOTE Some people also develop neurological complications such as meningitis, encephalitis or neuropathy. Typically the lymphocyte and CD4 counts are low during the acute illness.

Acute seroconversion illness is often the first sign of HIV infection.

1-35 Are people with seroconversion illness infectious to others?

Yes, during the first few weeks of HIV infection, especially if the person develops seroconversion illness, large amounts of virus are present in the blood and other body fluids, and the person is very infectious to others.

People are very infectious during the first weeks of HIV infection.

1-36 How are patients with acute seroconversion illness managed?

The patients are managed symptomatically with antipyretics (e.g. paracetamol) for fever.

1-37 What is the latent phase of HIV infection?

HIV infection and seroconversion are followed by a latent period when the person feels well. During this phase many people are not aware that they are HIV infected. Although there are usually no, or few, clinical signs during the latent phase of HIV infection, generalised lymphadenopathy is common.

During the latent phase the viral load is low and the CD4 count is normal or only mildly depressed.

Most people with asymptomatic HIV infection are not aware that they have been infected with HIV.

1-38 How long does the latent phase last?

Usually this silent, asymptomatic period lasts five to ten years in adults but it may last for as long as 15 years before the signs of AIDS appear ('slow progressors'). Occasionally, HIV-infected people progress rapidly to AIDS ('fast progressors').

The asymptomatic latent phase usually lasts five to ten years in adults.

1-39 What is symptomatic HIV infection?

When patients who have been clinically well during the latent (asymptomatic) phase of HIV infection become ill, they are said to have symptomatic HIV infection. The symptoms and signs of symptomatic HIV infection only present when the immune system is no longer able to protect the person from a wide range of viral, bacterial, fungal and parasitic infections (opportunistic infections).

Clinical illness only occurs late in the course of HIV infection.

1-40 When is symptomatic HIV infection called AIDS?

Once patients develop severe opportunistic infections or malignancies typically associated with HIV infection. This only occurs when the immune system has been severely

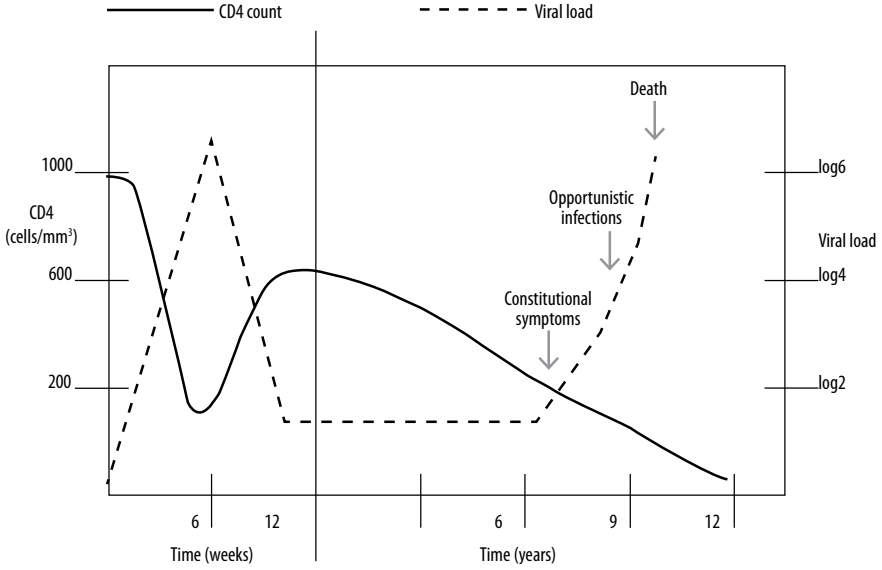

Figure 1-1: *The changes in viral load, CD4 count and clinical features of HIV infection*

damaged. Patients who are generally well or only mildly ill with HIV infection do not yet have AIDS.

1-41 How do the viral load, antibody levels and CD4 count change during the course of HIV infection?

The level of virus in the blood (viral load) rises very rapidly within weeks of infection due to the extremely high rate of viral multiplication. This temporarily depresses the CD4 count. The production of antibodies increases in response to the HIV infection. Antibodies, together with CD4 cells, attempt to control the amount of virus in the body and the levels of HIV in the blood decreases. Eventually (within six months) a balance is reached between the production and destruction of HIV. This is known as the viral set point.

With the onset of symptomatic HIV infection (constitutional symptoms) the CD4 count falls and the viral load increases and becomes very high with AIDS (opportunistic infections).

The level of virus in the blood is very high soon after infection and again with the development of AIDS.

NOTE A high viral set point carries a poor prognosis of rapid progression to AIDS, as it indicates failure by the immune system to control massive multiplication of HIV.

1-42 What clinical signs suggest the patient has HIV infection?

1. Unexplained weight loss
2. Unexplained fever or night sweats
3. Generalised lymphadenopathy
4. A variety of skin rashes
5. Mouth infections such as oral candidiasis
6. Chronic diarrhoea
7. Repeated respiratory infections or chronic cough
8. Signs of opportunistic infections and other HIV-related illnesses such as malignancies

Often painless, generalised lymphadenopathy in an otherwise healthy person is the first clinical sign of HIV infection.

Clinical stages of HIV infection

1-43 What is the natural progression of HIV infection?

The progression of early to advanced HIV infection usually follows a recognisable pattern which depends on the degree of damage to the immune system. The progression of HIV infection has been divided into 4 clinical stages by the World Health Organisation (WHO). Patients advance through stages 1 to 4 as their CD4 count falls.

The clinical signs become worse and the CD4 count falls as patients progress from stage 1 to stage 4 HIV infection.

A table of the World Health Organisation (WHO) stages of HIV infection is given at the end of this unit.

1-44 What are the clinical signs of stage 1 HIV infection?

Patients with stage 1 HIV infection are well and asymptomatic but almost all have persistent, generalised lymphadenopathy, especially in the neck, axilla and groin. Acute seroconversion illness is also included in stage 1. Therefore, stage 1 starts at the time of infection.

People with stage 1 HIV infection are generally well.

1-45 What are the clinical signs of stage 2 HIV infection?

Patients with stage 2 HIV infection have repeated minor problems. Skin rashes and minor mouth problems are very common. Often there is some weight loss (less than 10%) and mild diarrhoea can be a problem. Patients with these early stages of HIV infection can usually continue their daily activity.

Patients with stage 2 HIV infection have repeated minor clinical problems.

1-46 What are the features of stage 3 HIV infection?

Common features are unexplained weight loss (more than 10%), fever, oral candidiasis and diarrhoea. Pulmonary TB and severe bacterial infections indicate stage 3 infection. These patients feel generally unwell and are no longer able to continue with their usual daily activities. Most of these patients will improve if their opportunistic infections are treated.

Pulmonary TB and serious bacterial infections are common in patients with stage 3 HIV infection.

1-47 How would one recognise a patient with stage 4 HIV infection?

Marked weight loss continues and many patients are bedridden. Severe opportunistic infections such as oesophageal candidiasis, extrapulmonary TB, pneumocystis pneumonia, cryptococcal meningitis and toxoplasmosis are common. Anaemia and malignancies associated with HIV infection are also common. Patients with stage 4 disease are regarded as having AIDS. Response to antiretroviral treatment is usually good. Without treatment many will die within months.

Serious opportunistic infections are common when stage 4 HIV infection (AIDS) is reached.

1-48 What are the features of terminal AIDS?

Additional opportunistic infections such as CMV retinitis and avium TB can occur. Severe wasting and dementia are common. These patients are seriously ill, usually with a CD4 count below 50 cells/μl. Response to antiretroviral treatment may be poor as the immune system has been very

seriously damaged by HIV. Without treatment most patients rapidly die.

Common complications of HIV infection

1-49 What is an AIDS-defining illness?

A serious clinical condition which is very uncommon in HIV-negative people and yet seen commonly in patients with advanced HIV infection. Severe opportunistic infections and malignancies in HIV-positive patients are AIDS-defining illnesses. Common AIDS-defining infections include oesophageal candidiasis, and infections with pneumocystis, cryptococcus and toxoplasmosis.

1-50 Is pulmonary tuberculosis an AIDS-defining illness?

Although pulmonary TB is common in patients with HIV infection, and indicates stage 3, it also occurs in HIV-negative people and it is therefore not an AIDS-defining infection. In contrast, extrapulmonary TB is rare in HIV-negative people and is therefore an AIDS-defining illness.

1-51 What infections of the mouth are common with HIV infection?

The mouth and tongue are commonly affected when the immune system is damaged by HIV infection.

1. The commonest mouth condition is oral candidiasis (thrush).
2. Oral hairy leucoplakia. This is usually asymptomatic and painless, and presents as multiple, vertical white stripes along the side of the tongue. Its presence indicates immune depression.
3. Aphthous ulcers. These are very painful, shallow ulcers that can occur anywhere in the mouth.
4. Herpes simplex ulcers may also affect the mouth and are also painful.
5. Gum infections around the base of the teeth (gingivitis) which may cause pain and bleeding.
6. Kaposi's sarcoma.

NOTE Oral hairy leucoplakia is due to infection with the Epstein-Barr virus.

Severe oral infections which prevent the patient eating and drinking, and do not improve in a few days, may lead to further weight loss, dehydration and under-nutrition. These patients should be referred to a special HIV clinic.

1-52 What skin rashes are commonly seen in patients with HIV infection?

Many different skin rashes are seen in HIV-infected patients and a skin rash may be one of the earliest signs of a depressed immune system:

1. Pruritic papular eruption (PPE or 'itchy bump disease')
2. Seborrhoeic dermatitis
3. Fungal infections of the skin, hair and nails
4. Molluscum contagiosum
5. Warts
6. Impetigo and folliculitis
7. Severe, extensive scabies
8. Psoriasis
9. Shingles

Rashes may also be due to drugs used in antiretroviral treatment (e.g. nevirapine) or drugs used to treat opportunistic infections (e.g. co-trimoxazole). Drug reactions are more common in HIV-infected patients than in people who are not HIV infected.

1-53 What is characteristic of rashes in HIV-positive patients?

Rashes are often severe, chronic or recurrent, and respond poorly to standard treatment. Rashes frequently are atypical and usually do not resolve spontaneously. Previous rashes may become worse with the development of HIV infection, e.g. psoriasis, acne and eczema. With antiretroviral treatment most rashes disappear.

1-54 What is pruritic papular eruption (PPE)?

This is very common in patients with HIV infection and presents with a severe itch and scattered pigmented papules, especially on the trunk and limbs. It is difficult to treat and responds poorly to topical steroids and anti-itch agents.

1-55 What is wasting disease?

Before the advent of antiretroviral treatment, this was a common presentation of AIDS in patients in Africa. Weight loss is severe and associated with chronic diarrhoea. The patients feel weak and have fever. All patients with unexplained weight loss must be screened for HIV infection.

All patients with unexplained weight loss must be screened for HIV infection.

NOTE Severe wasting is due to anorexia, diarrhoea, malabsorption and infections as well as oral conditions which make eating painful (e.g. thrush or herpes).

1-56 What malignancies are associated with AIDS?

Some form of cancer occur more frequently in patients with AIDS. Viral infections and a damaged immune system are probably the cause. Of interest is that only some cancers are more common in AIDS patients. However, the progression of other cancers common in the general population is more rapid in AIDS patients. Cancers more common in patients with AIDS are:

1. Kaposi's sarcoma
2. Non-Hodgkin's lymphoma
3. Cervical cancer

Patients with any of these cancers must be tested for HIV infection.

Kaposi's sarcoma, non-Hodgkin's lymphoma and cervical cancer are more common in patients with AIDS.

1-57 What is Kaposi's sarcoma (KS)?

This is the most common cancer complicating AIDS.

Kaposi's sarcoma usually presents with multiple pink or purple patches in pale skins and brown or black patches

in dark skins, or nodules (bumps) on the skin, especially the face, trunk and legs. The mouth may also be involved, especially the hard palate. The prognosis is poor in advanced cases when organs such as the gut, lungs and lymph nodes are affected (visceral Kaposi's sarcoma). Non-visceral (skin) Kaposi's sarcoma is usually not life-threatening, but can become extensive and have an unacceptable appearance. The patches and nodules often improve with antiretroviral treatment.All patients with Kaposi's sarcoma should start ART within one week of presenting to the clinic. Mild cutaneous KS may respond to ART alone while extensive KS requires chemo or radiotherapy. All patients with extensive skin lesions, oral lesions or signs of disseminated KS should be referred to a KS or specialist clinic within 2 weeks of starting ART.

Kaposi's sarcoma presents with purple or brown skin patches or nodules.

NOTE Kaposi's sarcoma is associated with the Human Herpes 8 virus which may be sexually transmitted.

1-58 What is non-Hodgkin's lymphoma?

This is the second commonest cancer in AIDS patients. Non-Hodgkin's lymphoma is a group of different types of lymphoma which often progress rapidly. Therefore, early diagnosis and treatment are important. Lymphoma usually presents with large firm lymph nodes at one or more sites, or abdominal masses together with weight loss and unexplained fever. Sites other than lymph nodes can be involved, especially the brain, liver, bone marrow and gut. Non-Hodgkin's lymphoma of the brain may present with a wide range of neurological conditions including headaches, convulsions, confusion and memory loss. Any patient with a suspected lymphoma must be referred for investigation. The prognosis is usually poor.

Lymphoma of the brain may present in AIDS patients with a wide range of neurological signs.

NOTE Most lymphomas in AIDS patients are of B cell origin and associated with Epstein-Barr virus infection.

1-59 What is the presentation of cervical cancer?

Cervical cancer is common in women with AIDS. In the early stages there are usually no symptoms or signs. Therefore all HIV-positive women must have an annual screen with a PAP smear or cervical inspection for cancer.

All HIV-positive women must be screened regularly for cervical cancer.

NOTE The human papilloma virus, which is associated with cervical cancer, is sexually transmitted and more common in HIV-positive women.

1-60 What neurological conditions are associated with AIDS?

Many neurological complications are seen in patients with AIDS. Neurological problems may also be due to drug side effects (e.g. peripheral neuropathy with isoniazid (INH)).

1. HIV encephalopathy
2. Cryptococcal meningitis
3. Bacterial meningitis
4. Tuberculous meningitis or tuberculoma
5. Toxoplasmosis
6. Non-Hodgkin's lymphoma

NOTE The spinal cord, peripheral nerves and muscles can also be involved.

1-61 What is HIV encephalopathy?

HIV infects the brain early in the course of HIV disease. Signs of HIV encephalopathy usually develop slowly and become more obvious when the patient has AIDS, especially in the advanced stage. Common signs of HIV encephalopathy are:

1. Poor concentration and short-term memory loss, eventually leading to dementia
2. Personality changes with depression, apathy, withdrawal or irritability
3. Weakness, tremors or clumsiness

Often there are no obvious abnormalities on examination of the central nervous system early in the disease. The worsening of HIV encephalopathy can be slowed with antiretroviral treatment.

NOTE CT and MRI scans with HIV encephalopathy reveal cortical atrophy. In contrast, scans in progressive multifocal leucoencephalopathy (PML) due to Creutzfeldt-Jakob infection show areas of white matter demyelination.

WHO staging system for HIV infection in adults and adolescents

Clinical stage 1

- Seroconversion illness
- Asymptomatic infection
- Persistent generalised lymphadenopathy
- Normal daily activity

Clinical stage 2

- Weight loss up to 10%
- Minor oral problems (recurrent mouth ulcers)
- Skin rashes
- Recurrent upper respiratory tract infections
- Herpes zoster (shingles)
- Symptomatic, but daily activity normal

Clinical stage 3

- Weight loss of more than 10%
- Chronic diarrhoea for more than one month
- Prolonged fever for more than one month
- Oral candidiasis
- Oral hairy leucoplakia
- Pulmonary tuberculosis
- Severe bacterial infection (e.g. meningitis, pneumonia)
- Bedridden for less than 50% of the day in the past month

- Unexplained anaemia (haemoglobin level below 8 g/dl), and or neutropenia (neutrophil count below 500/mm^3) and/or thrombocytopenia (platelet count below 50 000/ mm^3) for more than one month

Clinical stage 4 (AIDS)

- HIV wasting syndrome
- Pneumocystis pneumonia
- Oesophageal candidiasis
- Toxoplasmosis of the brain
- Cryptococcal meningitis
- Diarrhoea due to Cryptosporidiosis or Isosporiasis
- Cytomegalovirus (CMV) disease
- Extrapulmonary TB
- Chronic or disseminated herpes simplex
- HIV encephalopathy
- Recurrent pneumonia
- Kaposi's sarcoma, lymphoma or invasive cervical cancer
- Confined to bed for more than 50% of the day

Additional clinical criteria indicating stage 4 disease

- Idiopathic thrombocytopenic purpura (ITP)
- Thrombotic thrombocytopenic purpura (TTP)
- Autoimmune haemolytic anaemia
- HIV-associated nephropathy
- HIV-associated cardiomyopathy
- Severe HIV neuropathy or HIV myelopathy
- Refractory apthous ulceration
- All malignancies (unless early malignancy that is surgically resectable with low relapse risk)
- Multiple drug resistant tuberculosis (MDR TB) HIV-associated vasculopathy
- Diffuse infiltrative lymphocytosis syndrome (DILS) with severe symptoms
- Acute inflammatory demyelinating polyneuropathy (AIDP)/chronic inflammatory demyelinating polyneuropathy (CIDP) non-responsive to immunomodulatory therapy

NOTE These patients may be initiated on ART following consultation and recommendation from an infectious disease/ART unit specialist or specialist in these listed pathologies.

Case study 1

A healthy pregnant woman is found to be HIV positive. She asks how she probably became infected and whether HIV infection is common in pregnant women. She asks the nurse whether she will pass HIV on to her infant.

1. How is HIV usually transmitted in South Africa?

By penetrative heterosexual vaginal intercourse. The risk of HIV transmission is highest with anal intercourse in both men and women. The risk of HIV infection is much less with oral sexual contact. Kissing is probably safe.

2. Can HIV be spread by normal social contact?

No. HIV is not spread by touching, holding hands, hugging, coughing, sneezing, using swimming pools, toilet

seats or sharing cooking, drinking and eating utensils.

3. Can a person with HIV infection appear perfectly healthy?

Many people feel well without any clinical signs in spite of having asymptomatic HIV infection for many years.

4. Are they infectious during this time?

Yes. The danger is that many infectious people who feel well do not know that they have HIV infection.

5. How common is HIV infection in pregnant women in South Africa?

In 2011, almost 30% of pregnant women attending state antenatal clinics were HIV positive. This has increased from less than 2% in 1990.

6. What is the risk that this woman will pass HIV to her infant?

With a vaginal delivery and no antiretroviral prophylaxis, the risk of HIV transmission is 20%. The additional risk of mixed breastfeeding is 15%. With antiretroviral prophylaxis consisting of triple therapy for the mother during pregnancy and breast feeding and Nevirapine for the child during breast feeding the overall risk is less than 2%.

Case study 2

A young woman presents with fever, a sore throat, enlarged lymph nodes and a rash. She also feels generally unwell.

1. Could these signs and symptoms be due to HIV infection?

The presentation is typical of the acute seroconversion illness which occurs in 50% of HIV infected people. This condition usually presents two to six weeks after HIV infection and may be misdiagnosed as glandular fever.

2. Should she be treated with antiretroviral drugs?

No. While treatment may be an option in the future, currently patients are not usually treated during seroconversion except in the context of a clinical trial. Usually symptomatic treatment (e.g. paracetamol for fever) is all that is needed.

3. How can the clinical suspicion of HIV infection be confirmed?

By finding a positive screening test (usually a rapid test). The rapid test can be done in a primary-care clinic. A negative test may be repeated after two weeks if acute seroconversion illness is suspected. All patients must be informed and counselled and give consent before a rapid test is done.

4. What is the window period?

The period between HIV infection and a screening test becoming positive. In the window period the HIV blood test may be falsely negative (the test is negative but the person is infected with HIV). The window period usually lasts up to six weeks. Some people with acute seroconversion illness may still be in the window period.

5. How does HIV cause disease?

By killing CD4 cells and, thereby, damaging the immune system. As a result the body is unable to protect itself from a wide range of viral, bacterial, fungal and parasitic infections.

6. What effect is HIV having on society in Africa?

The HIV epidemic is having a devastating effect on society. It is estimated that over six million South Africans are HIV positive. Most are female.

Case study 3

A 25-year-old man is seen at a primary-care clinic with herpes zoster which is very painful. He has also lost some weight and complains of recurrent mouth ulcers. On examination he has generalised lymphadenopathy and typical pruritic papular eruption. His HIV test was positive four years ago when he was screened at work. He is still able to continue working.

1. How would you grade the clinical stage of HIV infection in this patient?

He should be graded as stage 2. Herpes zoster, recurrent aphthous mouth ulcers and skin rashes with mild weight loss are seen in stage 2 HIV infection. The rapid test confirms the clinical diagnosis. Patients in stage 2 can usually continue working.

2. What would the staging be if he only had lymphadenopathy and was generally well?

Stage 1.

3. What is pruritic papular eruption?

Pruritic papular eruption (PPE or 'itchy bump disease') is common in patients with symptomatic HIV infection. It presents with scattered pigmented papules (bumps) which are very itchy. The rash is usually seen on the trunk and limbs, it is difficult to treat and responds poorly to topical steroids but usually resolves completely after a few months of ART.

4. What other skin rashes are common in patients with stage 2 HIV infection?

Seborrhoeic dermatitis, molluscum contagiosum, warts, scabies and psoriasis. Bacterial and fungal infections are also very common.

5. What are common causes of a painful mouth in patients with HIV infection?

A painful mouth is a common complaint in patients with HIV infection. Recurrent aphthous ulcers, oral candidiasis, herpes ulcers and infected gums are frequently seen. Kaposi's sarcoma and oral hairy leucoplakia are usually not painful.

6. How long is the latent period?

This varies between people. However, many people with HIV infection remain well (asymptomatic) for about ten years (except for possible

acute seroconversion illness) before developing clinical signs and symptoms of HIV infection.

Case study 4

A woman presents with a cough and night sweats for six weeks and a number of painless, purple patches on her skin. She has oral thrush and difficulty swallowing. Her husband died of AIDS the year before. On testing she is HIV positive.

1. What is the most likely cause of the cough and night sweats?

She almost certainly has pulmonary tuberculosis.

2. What condition causes multiple, painless purple patches in a patient with HIV infection?

Kaposi's sarcoma. These patients may have multiple purple or brown skin patches or nodules. The mouth, lymph nodes, lungs and gut may also be involved.

3. Why is she having difficulty swallowing?

The finding of oral thrush (oral candidiasis) and difficulty swallowing suggests that she may have oesophageal candidiasis.

4. Does she have AIDS?

Yes. Both Kaposi's sarcoma and oesophageal candidiasis are AIDS-defining conditions as they are very rare in people with a normal immune system (i.e. they are opportunistic infections). She would therefore be graded as having stage 4 HIV infection – i.e. AIDS.

5. Is pulmonary TB an AIDS-defining illness?

No. If she only had pulmonary TB as a complication of being HIV infected she would be graded as stage 3. Extrapulmonary TB would make her stage 4.

6. What malignancies are associated with AIDS?

Malignancies associated with AIDS are Kaposi's sarcoma, non-Hodgkin's lymphoma and cervical cancer.

2

Managing people with HIV infection

Before you begin this unit, please take the corresponding test to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- Manage a well patient with asymptomatic HIV infection.
- List ways of developing a healthy lifestyle.
- Describe ways the community can play an important role in supporting people with HIV infection.
- Provide counselling for people with HIV infection.
- Monitor the CD4 count.
- Provide care to patients terminally ill with AIDS.

General management

2-1 What are the phases of managing patients with HIV infection?

1. Managing patients with acute seroconversion illness
2. Managing well people in the asymptomatic (latent) phase of HIV infection
3. Managing patients with symptomatic HIV infection
4. Preparing patients for antiretroviral treatment
5. Managing patients on antiretroviral treatment
6. Providing terminal care to patients with terminal AIDS

2-2 What are the goals of managing people who have asymptomatic HIV infection?

1. Keeping them well for as long as possible
2. Helping them live a normal, healthy lifestyle with a positive attitude
3. Preventing them from spreading HIV infection to others

2-3 What is the management of well people with asymptomatic HIV infection?

It is important that attention is paid to the following:

1. Education about HIV infection and AIDS
2. Practising safer sex
3. Taking a good, balanced diet
4. Exercising regularly

5. Having adequate rest
6. Developing a positive outlook on life
7. Avoiding smoking, drinking excess alcohol or abusing drugs
8. Getting emotional support and counselling if needed
9. Providing good primary healthcare

In summary, develop a healthy, positive lifestyle. This is a very important part of managing a person with HIV infection. Each person with HIV infection needs a wellness programme.

A healthy lifestyle is very important for people who are HIV postive.

2-4 What is a wellness programme?

This is an active programme to encourage HIV-infected people to remain physically and emotionally well for as long as possible. A wellness programme promotes a healthy lifestyle. Both regular follow-up by an HIV clinic and support from the community are important. The media (radio, TV, newspapers, magazines, books) also have a role to play in promoting wellness.

2-5 Why is education about HIV infection and AIDS important?

The most important step in helping people with HIV infection is to enable them to learn about and understand their disease. They need to feel that they are still in control of their own lives and can play an active role in managing their illness. They must be empowered to make the best decisions for themselves. A good understanding of HIV infection and AIDS helps to reduce their anxiety and develop confidence and hope.

Knowledge and understanding is power.

2-6 What education is needed?

1. The natural history of HIV infection
2. How to prevent infecting others
3. Ways of strengthening the immune system through healthy living
4. The early symptoms and signs of HIV infection
5. What can be offered with antiretroviral treatment

2-7 Why is it important for an HIV-positive person to practise safer sex?

1. To prevent spreading HIV to others.
2. To avoid reinfection with HIV. Being HIV positive does not prevent further infection with other strains of HIV. The progression to AIDS is more rapid with multiple HIV infections.

It is essential that HIV-positive people practise safer sex.

2-8 What is safer sex?

The only way of totally preventing the sexual transmission of HIV is to avoid sex. However, the risk of HIV infection can be greatly reduced by changing sexual practices (safer sex). Condoms must be used every time the person has sex. Avoid multiple partners. Anal

sex is particularly dangerous. Although oral sex is safer, it is still a recognised way of transmitting HIV.

The 'ABC' of safer sex is Abstinence (no sex), Be faithful (one partner only) and Condoms (always use a condom).

2-9 Are condoms adequate for contraception?

Condoms are only partially effective as contraception. Therefore some other form of contraception must be used as well. Progesterone injections (e.g. Petogen three-monthly or Nur-Isterate two-monthly) are best as some medication taken by HIV-infected people may interfere with oral contraceptives (the pill).

Any HIV-infected woman planning to fall pregnant should get advice from an HIV clinic.

2-10 Why is diet, rest and exercise important?

Having a good diet, adequate rest and keeping fit with moderate exercise help to maintain the normal function of the immune system. It is important that people in the latent phase look after their health and wellbeing. This will prolong the period of asymptomatic HIV infection.

2-11 Why is it important to maintain normal body weight?

Because marked weight loss and poor nutrition are associated with a rapid progress to AIDS. Malnutrition weakens the immune system.

Weight loss in HIV-infected people may be due to:

1. Poverty
2. Depression
3. Poor appetite due to illness
4. Oral and oesophageal candidiasis
5. Chronic diarrhoea
6. Gut malabsorption
7. Tuberculosis

Unintentional weight loss is often an early sign of symptomatic HIV infection. It is important to maintain normal body weight for as long as possible.

2-12 What dietary advice should be given?

A balanced diet is important to provide sufficient amounts of carbohydrates, fats and protein. A diet containing an adequate supply of vitamins and trace elements may be supplemented with a daily multivitamin pill. A good calorie and protein intake helps to prevent weight loss.

First the person's present diet and pattern of eating should be reviewed. Then the person can be advised on local, affordable foods which would improve the diet. Small frequent meals are best. Alcohol intake should be reduced or stopped and smoking discouraged. The nutritional value of meals can be improved by:

1. Using starchy foods as the basis of most meals to provide calories, e.g. porridge, samp (mielies), rice or potatoes.
2. Adding 1–2 teaspoons of vegetable oil, margarine or peanut butter to provide added calories.

3. Using whole wheat or brown bread rather than white bread.
4. Providing protein with fish, eggs and meat (expensive) or beans, peas, lentils or soya products (cheaper).
5. Using only a little fat and salt.
6. Buying fruit in season (expensive) or fresh vegetables (cheaper). Do not overcook vegetables as this damages vitamins.
7. Use a variety of foods mixing starch, protein, vegetables and fruit. Cultivating a vegetable garden can save costs.

A good diet need not be expensive and helps to improve and maintain the immune system.

NOTE Good trials of dietary supplements are still needed. There is some evidence of a potential beneficial effect of vitamins and other micronutrients on the immune system of patients with HIV and they may be prescribed in addition but not instead of ART. There is little scientific evidence that supplementation with specific nutrients is of benefit. Multivitamin supplements should not exceed two to three times the recommended daily allowance.

2-13 Can HIV infection be managed without antiretroviral treatment?

It is very important for all HIV-infected people to understand that every effort must be made to prolong the latent phase and delay the onset of symptomatic HIV infection. Antiretroviral treatment is only recommended when HIV becomes symptomatic or when the patients CD4 is less than 350 cells/mm^3.

Many of the symptoms of AIDS can be relieved and HIV-associated infections can be treated. However, antiretroviral treatment is the only effective management of AIDS and offers the only hope of prolonging a good quality of life.

2-14 Are herbal medications of value in HIV infection?

Many plants have an effect on the immune system. Some are believed to be helpful while others have been shown to depress the immune system. However, only very limited clinical trials have been conducted, with mixed results. It is hoped to identify herbal compounds which may strengthen the immune system and delay the onset of AIDS. Plant and other non-medical (alternative) substances can have serious side effects. They may also interfere with antiretroviral treatment.

NOTE It has been shown that plant sterols and sterolins interact with antiretroviral drugs and lower blood levels. Until the proper tests are done they cannot be recommended.

2-15 What primary healthcare is needed by people who are HIV positive?

1. Promoting a healthy lifestyle
2. Offering primary prophylaxis when indicated
3. Providing an immunisation service
4. Monitoring the patient's weight
5. Screening for the early symptoms and signs of symptomatic HIV infection
6. Managing the minor problems associated with HIV infection

7. Helping patients obtain social support and counselling when needed
8. Monitoring the CD4 count

2-16 What is primary prophylaxis?

Most of the morbidity and mortality in HIV-infected patients are due to HIV-associated infections. Primary prophylaxis is the use of specific antibiotics to prevent some of these infections. Therefore primary prophylaxis is an important part of healthcare during the asymptomatic phase of HIV infection.

Co-trimoxazole and INH are the most important drugs used for primary prophylaxis.

NOTE Secondary prophylaxis is the use of specific preventative antibiotics in patients who have previously been infected with that organism.

2-17 What immunisations are helpful?

Most adults will have received the routine schedule of childhood immunisations. Some additional immunisations may be helpful in well people with HIV infection:

1. Hepatitis B
2. Influenza

The influenza immunisation is not effective in people with a CD4 below 200. Unfortunately these immunisations are expensive and are not always available from state clinics.

2-18 What is the risk of malaria in HIV-positive people?

The risk of severe malaria is increased in people infected with HIV. Therefore malaria is a major cause of death in HIV-infected people in some countries. If possible, they should avoid entering known malaria areas. Avoid mosquito bites by using insecticide-impregnated bed nets and insect repellents. Stay indoors from late afternoon to midmorning and wear long sleeves and trousers as well as shoes.

Prophylactic drugs are recommended. Co-trimoxazole helps reduce the risk of malaria. Treat immediately if symptoms of malaria develop within a few weeks of entering a malaria area.

NOTE Prophylaxis with mefloquine, doxycycline or 'Malanil'. Treat malaria with quinine and doxycycline or 'Coartem' (artemethet and lumefantrine).

2-19 Should HIV-positive patients bring their sexual partners to the clinic?

HIV-positive patients should bring their sexual partners, husband or wife, and children to the clinic for HIV counselling and testing (HCT). Screening all high-risk groups of people for HIV infection is important in limiting the spread of infection. Ideally everyone should be screened.

The role of the community

2-20 Can the community play an active role in managing HIV-positive people?

If the HIV epidemic is to be controlled and patients with HIV infection adequately managed, the community will have to become actively involved in all aspects of prevention, support and care. This is difficult where poverty, gender inequality, stigma and discrimination are common and HIV-infected people see themselves as helpless victims.

Local communities must take ownership of their joint problem and not simply rely on government providing the services. Fear, denial, stigma and discrimination will have to be overcome before a communal sense of responsibility can be developed and people believe they can contribute positively to solving the problem and make a difference.

Communities must become actively involved in addressing the enormous problem of HIV infection and AIDS.

Prevention and management of HIV infection must be seen as parts of the same integrated community programme. One will not be effective without the other.

2-21 What active role can the community play?

1. Changing sexual attitudes and behaviour
2. Reducing the stigma of HIV infection and AIDS
3. Supporting people living with HIV and their carers
4. Working with government services, non-government organisations and volunteer groups
5. Helping patients access health services and welfare grants
6. Educating the community about AIDS and helping to promote open discussion about HIV infection
7. Helping to empower women
8. Help care for AIDS orphans
9. Advising healthcare services on caring needs

The community has a very important part to play in the prevention and management of HIV infection.

2-22 Which community members can play an active role in helping?

1. Families
2. Friends and partners
3. Church groups
4. Youth clubs
5. Trade union organisations
6. HIV support groups
7. Other social groups
8. Volunteer health workers

Everyone in the community has a part to play. Without a community partnership, health services will have only a limited impact in preventing

HIV infection and managing people with HIV infection.

2-23 What is an HIV support group?

One of the best ways of supporting someone with HIV infection is for them to join a group of people who also have HIV. Here they can share experiences in a safe, non-judgemental environment. Members of support groups can bring education, hope and improve the quality of life.

2-24 What are volunteer health workers?

These are members of the community who want to help people who are living with HIV. Home nursing is the greatest need. Patients need to be fed, cleaned, comforted and cared for. Help with simple chores such as cooking, cleaning, shopping and collecting water and firewood make a big difference.

Provision of knowledge, skills and support for lay health volunteers is essential. Volunteer health workers are the most realistic way of providing home-based care. They also play an important role in reducing stigma and discrimination in the community.

2-25 What is stigma?

Stigma is the negative thoughts and feelings that people have. It is a form of discrimination and has an important negative effect on people with HIV infection and their families. Unfortunately stigma is common and causes great personal suffering. It remains one of the most difficult obstacles in tackling the HIV epidemic.

Stigma is a negative, damaging attitude towards people who are HIV positive.

2-26 What are the effects of stigma?

People with HIV who are stigmatised feel lonely, helpless and afraid. They are made to feel bad, despised, embarrassed and shameful and may hate themselves. They often feel that they are no longer respected and have brought disgrace on themselves, their family and their community because they are HIV positive. Due to stigma and discrimination, people with HIV are often avoided, feel socially isolated, and stop seeing friends and family. They may be thrown out of their homes, sacked from their jobs, abandoned by friends and even assaulted or killed.

Owing to the effects of stigma and fear of discrimination, many people refuse to be tested for HIV or deny their HIV status. This often leads to a fear of disclosure, delay in treatment and failure of preventing the spread of HIV. Some people choose to die of AIDS rather than disclose their HIV status and seek treatment. In many societies the words 'HIV' and 'AIDS' are not even used. People deny there is anyone with AIDS in their community despite the fact that everyone knows that many people are dying of HIV.

Stigma results in fear, denial and failure to prevent the spread of HIV.

Owing to the fear of stigma, the HIV status of pregnant women is often not

recorded on the antenatal cards, while that of their infants is not recorded on their Road-to-Health cards. This prevents essential communication between healthcare workers.

2-27 What are the causes of stigma?

Usually ignorance and fear. The stigma towards HIV infection is usually due to the stigma surrounding sex and sexual activity. Stigma to sex is the real problem. In many societies, sex is seen as shameful and not spoken about or even acknowledged. Sex and the use of condoms are 'taboo' subjects. Negative attitudes towards sex are often promoted by the male head of the family, traditional leaders and the church. Many believe that the immorality of young women is the cause of the HIV epidemic. It may even be viewed as a punishment to society for the sin of promiscuity.

NOTE In a patriarchal society, sexual relations are controlled by men, leaving women disempowered and unable to control their own sexuality. Unequal power relations prevent women from protecting themselves and their children against HIV.

2-28 What can be done to overcome stigma?

Education, understanding, and critical and open discussion are the most effective ways of preventing and overcoming stigma. People need to learn appropriate emotional responses to sex and HIV infection. Support groups, where sexuality and HIV infection can be debated, are of great help and support.

Groups such as the Treatment Action Campaign and LoveLife have tried to make people aware of the damage that is being done by stigma to HIV. Life skills training at schools could reduce stigma to HIV by teaching healthy, open attitudes towards sexuality and the risk of sexually transmitted diseases. Government, church and community leaders, sports people and entertainers who are HIV positive need to disclose their status.

It is essential to create a social climate where people are not afraid of admitting they have HIV. Then they can openly practise safer sex and seek healthcare.

Counselling

2-29 What is counselling?

Counselling is a process of education, communication and support by which a counsellor helps people to cope with difficult situations in their lives so that they are able to make important decisions and find realistic ways to solve their problems. Counselling, therefore, helps people make their own choices and supports these decisions, rather than simply giving them advice and information or telling them what to do. Counselling is far more than simply educating and is best provided by a trained counsellor.

Counselling is about empowering people to make important decisions and to solve their own problems.

2-30 What is a counsellor?

A counsellor is someone who is trained to educate, assist and give psychosocial support to people with problems. A good counsellor helps people to understand and accept their HIV status and to take the best course of action to lead a positive life.

Either a professional healthcare worker (nurse, social worker, doctor) or a lay person can be trained as a counsellor. Training large numbers of good lay counsellors is one of the major challenges facing those who care for people with HIV infection.

Both professional and lay people can be trained to be good counsellors.

2-31 What counselling may be needed?

Patients with HIV infection have many concerns about their future. Once they understand the nature of HIV infection and know that their immune system will become progressively damaged, they need to be able to speak about their worries and fears and obtain good information. They need good counselling.

2-32 When is counselling needed?

Counselling is needed:

1. When a person is being prepared for an HIV screen. Counselling is also needed when the person is told the result of the test, whether positive or negative.
2. During the asymptomatic phase of HIV infection when people are trying to practise a healthy lifestyle.
3. During the symptomatic phase when people have to learn to live with their illness.
4. During preparation for antiretroviral treatment and again while they are on treatment to ensure good adherence.
5. During terminal care when they are preparing to die.

2-33 What important skills are needed for HIV counselling?

Two essential skills are needed for HIV counselling:

1. A good knowledge of HIV infection and the personal implications of being infected with HIV.
2. The ability to communicate effectively. Communication is the basis of good counselling.

2-34 What is effective communication?

Communication in counselling is a two-way process in which information, knowledge, thoughts and ideas are passed between the person being counselled and the counsellor. The spoken word is the most important means of communication but the counsellor must be aware that people may also pass important messages by showing their emotions and in their body language (how they act). The counsellor must learn to pick up these signs as it helps in gathering information and giving appropriate understanding (empathy) and emotional support. Effective

communication requires the skill of active listening.

Effective communication is a combination of active listening and using words with care and consideration.

2-35 What is active listening?

Active listening is the process of hearing not only the words people say, but also noting their body language and emotional reactions, and trying to understand the meaning behind their words and actions. In order to understand what a person is saying and to respond appropriately, the counsellor must become skilled in actively listening to people.

Active listening is the key to effective counselling.

2-36 What are the steps to good counselling?

A good counsellor should:

1. Put the person at ease so that they can feel free to talk.
2. Remove distractions and concentrate on what is being said. Close the door. Do not take phone calls, fiddle with notes or tap your pencil.
3. Speak a language that the patient can understand (or use a competent translator).
4. Do not talk too much. You cannot listen if you keep talking. Be silent when silence is needed. Do not interrupt unnecessarily or finish people's sentences.
5. Show interest.
6. Be patient and allow questions.
7. Express empathy and understanding. Try to put yourself in their place so that you can see the problem from their point of view.
8. Help people being counselled to identify problems and try to understand the causes before encouraging them to develop ways of finding solutions.
9. Always keep personal information confidential.

2-37 What are common errors which prevent good counselling?

1. Talking more than listening
2. Interrupting and arguing
3. Being judgemental
4. Concentrating only on facts, not feelings
5. Talking too fast and using complicated medical language

'If you do not listen to the person being counselled, do not expect them to listen to you.'

Good communication is blocked when the counsellor is judgemental, critical, threatening, manipulative, uninterested, or tries to control the discussion.

2-38 What else can help effective communication?

1. Choose your words carefully to ensure that what you say is what the person being counselled will understand.

2. Say what you mean and give simple messages.
3. Remember that as you can receive messages from the person being counselled from their body language, emotional reactions and tone of voice, so can you pass messages to them in the same way. Make sure you pass the 'right' message.
4. Repeat important information and make sure it is understood. Some messages may need to be repeated many times at one or more visits before they are accepted and understood.

Monitoring immune function

2-39 What test is used to measure the degree of damage to the immune system by HIV infection?

The CD4 count. CD4 cells are lymphocytes that play a very important role in the normal functioning of the immune system. HIV attaches to CD4 cells and kills them. As a result the number of CD4 cells gradually falls as the HIV infection progresses and more and more CD4 cells are killed. Therefore the CD4 count is the best measure of the degree that HIV has damaged the immune system.

The CD4 count measures the degree of damage done by HIV to the immune system.

2-40 What is a normal CD4 count?

The normal CD4 count in HIV-negative, healthy adults is 500 to 1500 cells/µl. As the CD4 count falls below 500 cells/µl the function of the immune system steadily becomes worse and the patient is at increased risk of many infections.

The normal CD4 count is above 500 cells/µl.

2-41 What is the predictive value of a low CD4 count?

The lower the CD4 count, the greater the risk of symptomatic HIV infection and AIDS. Therefore, the CD4 count is the best predictor of the risk that an HIV-positive person will develop severe HIV-associated infections (i.e. AIDS).

The 2013 South African guidelines recommend that antiretroviral treatment should be offered when the CD4 count falls below 350 cells/µl. However, antiretroviral treatment should also be offered to all people with Stage 3 or 4 HIV diseases and all pregnant women and people with TB irrespective of their CD4 count.

The CD4 count also indicates how quickly a person will progress to symptomatic HIV disease.

2-42 How fast does the CD4 count fall?

In most HIV-infected people who are not on antiretroviral treatment, the CD4 count falls each year by

approximately 25 to 50 cells/µl. This will result in the CD4 count falling from 600 to 200 in four to eight years. Most HIV-positive people will have symptoms and signs of HIV infection by the time the CD4 count has reached 200 cells/µl.

In some people the CD4 count falls particularly fast (rapid progressors) while in others it falls slower than usual (slow progressors).

2-43 How accurate is the CD4 count?

The CD4 count is generally an accurate measurement. However, the CD4 count may vary, therefore the test should be repeated if the result is unexpected. Temporary falls may be due to an acute illness or recent vaccination.

2-44 How often should the CD4 count be measured?

In HIV-positive people who are well, the CD4 count should be measured every 6 months to assess the condition of the immune system. Antiretroviral treatment should be started when the CD4 count falls below 350 cells/µl. Regular monitoring of the CD4 count is an important part of the management of people with HIV infection.

NOTE The CD4 count is best done in stable patients who are not acutely ill with HIV-associated or other infections.

The CD4 count is the best way of monitoring the progress of HIV infection.

2-45 Should the viral load be monitored in well patients?

There is no need to routinely measure the viral load in patients with HIV infection who are not yet on antiretroviral treatment. Regular measurements of viral load are used to monitor the response to antiretroviral treatment.

NOTE A high viral load (above 100 000 copies/ml) indicates a high risk for disease progression.

There is no need to routinely measure viral load in patients who are not on antiretroviral treatment.

Palliative and terminal care

2-46 What is palliative care?

Palliative care is the care of patients who have an incurable disease (such as HIV infection). It aims at reducing suffering and improving the quality of life in these patients. Palliative care starts at the time of the diagnosis and addresses all the patient's physical, emotional, social and spiritual needs. Although HIV infection cannot be cured, most of the HIV-associated conditions can be prevented or adequately treated and controlled.

Palliative care addresses the physical, emotional, social and spiritual needs of people with an incurable disease.

NOTE Palliative care aims to 'heal' when a cure is no longer possible.

2-47 What is terminal care?

In contrast, terminal care is the active care of patients whose disease no longer responds to treatment, e.g. antiretroviral drugs. Terminal care is not the same as no care or poor care. Patients who are dying of AIDS need terminal care. Care should never be withdrawn because there is no longer any hope for a cure.

2-48 Do patients with advanced HIV infection need terminal care?

As HIV infection cannot be cured there is an enormous need for terminal care in these patients. Terminal care is most needed in patients who are likely to die within months or weeks.

2-49 Where should terminal care be provided?

Home care is the basis of terminal care. If at all possible these patients should be cared for in their own home where they are comfortable in their own surrounding and with their family and friends. Only if this is impossible should they be given care in an institution, preferably in a hospice.

Terminal care should be provided at home if possible.

2-50 What is a hospice?

This is a place where terminally ill patients can be cared for. Management is aimed at compassionate care and support rather than cure. Members of a hospice team also help to care for patients who are at home.

2-51 Who should provide terminal care?

As there are so many aspects to terminal care, it is best provided by a team of people who are trained in this special type of care. A multidisciplinary approach is needed to meet the many different physical, psychosocial and spiritual needs of terminally ill patients. Patients, family and friends also have a role in terminal care.

2-52 What are the goals of terminal care?

To improve the quality of care of patients, and their families, who are facing death. Terminal care offers prevention and relief of suffering. The goal of terminal care is not necessarily to prolong life, but to reduce suffering.

The goal of terminal care is to prevent and relieve suffering.

2-53 What does terminal care involve?

1. The controlling of unpleasant symptoms, especially pain
2. Reducing the side effects of drugs used
3. Treating HIV-associated infections
4. Supporting the patient as well as family and friends
5. Giving patients and families control over the patient's management

2-54 What physical problems need to be addressed with terminal care?

1. Nutrition
2. Pain and discomfort

2-55 What are the nutritional needs in patients with terminal AIDS?

These patients are often wasted and very underweight. They may also have a poor appetite, nausea and difficulty swallowing. It may be difficult for them to obtain and prepare food.

High-calorie and protein foods are important. It is important that patients are able to choose foods which they prefer. If possible, intravenous fluids or nasogastric feeds should be avoided.

2-56 Is pain a common problem in patients with advanced AIDS?

Yes, severe pain is very common in patients who are dying of AIDS. It is likely to be under-diagnosed and under-treated. Pain significantly reduces the quality of life and results in fear and despair. Pain also causes distress to the family.

Severe pain is a major problem in patients who are dying of AIDS.

2-57 What are the principles of pain relief?

1. The correct choice and dose of analgesia (pain relief) is important.
2. Analgesics (drugs to relieve pain) should be given regularly ('by the clock') to both prevent and treat pain.
3. Oral analgesia should be used whenever possible.
4. Give clear written instructions.
5. Assess the amount of pain and review the pain management frequently.
6. Manage factors that aggravate pain such as fear, loneliness and depression.

The aim of pain management is to control pain by giving analgesia regularly so that pain can be prevented.

The aim of pain management is to prevent pain.

2-58 What common mistakes are made in treating pain?

1. Morphine is used too late.
2. The dose of analgesic is too low.
3. Medication is not given frequently or regularly enough.
4. Medication is only used to treat, rather than prevent, pain.

2-59 What common analgesics are used to control pain?

1. **For mild pain**: Paracetamol (Panado) and ibuprofen (Brufen). The dose of paracetamol is 1000 mg (2 x 500 mg tablets) every four to six hours as required. The dose of ibuprofen is 200 to 400 mg every four to six hours as needed.
2. **For moderate pain**: Codeine phosphate 30 to 60 mg every four hours. Often paracetamol or ibuprofen is used in addition.
3. **Severe pain**: Oral morphine solution starting at 5 to 10 mg every four hours.

The choice of analgesics for an individual depends on their degree of pain. As pain increases one moves up the 'treatment ladder' from step 1 (non-opioids such as paracetamol and ibuprofen) to step 2 (weak opioids such as codeine phosphate) to step 3 (strong opioids such as morphine).

NOTE Amitriptyline (an antidepressant), carbamazepine, gabapentin and pregabalin (anticonvulsants) and steroids are often helpful for pain due to peripheral neuropathy, herpes neuralgia or nerve compression.

2-60 How is morphine used?

If possible, it should be given orally. A dose must be given every four hours as the action of morphine is short. Give an extra dose equivalent to the four-hourly dose if the pain is not controlled. Giving extra doses for 'breakthrough' pain is very important. The starting dose of 5 to 10 mg should be increased by 50% every second day until the pain is controlled (the total dose over 24 hours should be divided by two to give the amount that the daily dose should be increased). There is no maximum dose. The correct dose is the dose which is effective. Therefore the dose of morphine should be titrated against the degree of pain.

Morphine can also be given by continuous subcutaneous infusion with a syringe driver, intramuscularly or intravenously.

Frequent doses of oral morphine are the most effective form of pain relief.

2-61 What common problems occur with morphine?

1. All patients on morphine develop constipation. Fruit, bran and extra fluids are helpful. Laxatives such as liquid paraffin 5 to 20 ml daily and senna (Sennacot) 15 to 30 mg daily should be used. Constipation does not become less with continued use of morphine and is the major side effect. Morphine may be useful in controlling chronic diarrhoea.
2. Nausea and drowsiness. This improves with time (tolerance) and responds to a lower dose.

Addiction is not of concern when morphine is used to control pain in terminally ill patients. Do not stop morphine suddenly as this may result in withdrawal symptoms. Respiratory depression is uncommon when morphine is used to control pain.

2-62 What other forms of discomfort are common in advanced HIV infection?

1. Anorexia, nausea and vomiting
2. Diarrhoea
3. Constipation
4. Cough and shortness of breath
5. Itch or dry skin
6. Fatigue and weakness
7. Lack of sleep
8. Bed sores
9. Incontinence

A syndromic approach is used in terminal care when the symptoms are managed even if the underlying cause cannot be treated. Help from hospice staff is very useful in preventing and managing most of these problems.

2-63 What can be used to treat nausea?

Nausea is a common problem, especially when treatment with morphine is started. Metoclopramide (Maxolon) 10 mg orally eight-hourly is helpful.

2-64 How can treating HIV-associated infections improve the quality of life in a patient dying of AIDS?

Treating the symptoms caused by HIV-associated infections can greatly improve the quality of the last weeks of life. For example, treating painful mouth ulcers, or relieving painful swallowing by managing fungal oesophagitis, or preventing blindness due to CMV retinitis.

Relief of symptoms is often best achieved by treating HIV-associated infections.

2-65 Is it worthwhile treating patients who are dying?

Yes. Patients should never be allowed to feel abandoned by their health carers. Pain, discomfort and distress must always be aggressively managed. However, sometimes it may not be realistic to treat terminally ill patients if the treatment will only prolong their suffering.

The question that must always be asked is 'will this make a difference to the quality of the person's life?'

2-66 What are the psychological aspects of terminal care?

Anxiety, fear and depression are common in terminally ill patients and are often not recognised. It is important to manage anxiety and depression as they both aggravate pain.

Anxiety, fear and depression make pain worse.

2-67 What are the signs of depression?

Withdrawal, sadness, sleep disturbances, poor appetite, depressed mood, lack of energy and interest in the world around them, and suicidal thoughts. Depression is common and unfortunately often missed. Management consists of emotional support and antidepressants. Response to medication may take a few weeks.

2-68 What is a memory box?

This is a simple box that parents can store mementos in for their children. Photographs, letters and cards are kept in the box which is given to the children when they are older to help them remember a parent who has died of AIDS. A memory box is one of the many ways that a parent can prepare themselves before death separates them from their children.

2-69 How can the spiritual needs of terminal patients be met?

Most people as they near the end of their lives need to speak to someone about their approaching death. The spiritual

needs of members of a religious group usually are well attended to. However, many people who have not regarded themselves as religious also need spiritual counselling. It is important for the members of the health team to find someone suitable to meet this need.

2-70 Do the carers need care themselves?

Yes. This is often forgotten or not realised. Care of the carers is a very important part of terminal care. It is physically and emotionally exhausting to care for terminally ill patients. Practical help with lifting, turning, washing and feeding is needed, as well as emotional support.

Case study 1

A young woman with asymptomatic HIV infection is referred to a primary-care clinic where the staff have a special interest in managing HIV-positive people who are still well. She wants to learn how to live with her condition.

1. What are the goals of managing people who have asymptomatic HIV infection?

To help these people to remain well for as long as possible and teach them how to live a healthy lifestyle. They also need to prevent spreading HIV infection to others.

2. What should she do to develop a healthy lifestyle?

Take a balanced diet, get adequate rest and regular exercise. Avoid excessive alcohol, do not smoke or abuse drugs and develop a positive outlook on life.

3. How can she get help to achieve these goals?

She can join a wellness programme.

4. What is an HIV support group?

This is a group of people with HIV infection who can support each other and share experiences in a safe, non-judgemental environment. They can learn from one another how to live a healthy life.

5. What is safer sex?

Abstinence is the only way to be completely safe. However, being faithful to a single partner and using a condom are ways to greatly reduce the risk of getting or passing on an HIV infection.

6. Can HIV infection be managed without antiretroviral treatment?

Much can be done to remain well for many years after HIV infection. Minor problems can also be successfully managed. However, antiretroviral treatment is the only effective management when a patient develops AIDS.

Case study 2

A healthy man with asymptomatic HIV infection has been followed up at a local clinic for a number of years. At his last visit his CD4 count is 650 cells/μl.

1. Is his CD4 count normal?

Yes, as the normal range is 500 to 1500 cells/µl.

2. When should his CD4 count be repeated?

A patient with asymptomatic HIV infection should have a routine CD4 count measured every 6 months.

3. How fast does a CD4 count fall?

The rate of fall varies from one person to another. However, the CD4 count in most HIV-infected people falls by 25 to 50 cells/µl each year.

4. Should the viral load also be measured?

The viral load is not routinely measured unless the person is being managed on antiretroviral treatment.

5. What is the value of measuring his weight at each clinic visit?

Unexpected weight loss may be an early sign of symptomatic HIV infection or tuberculosis. Maintaining a normal body weight by taking a good, balanced diet helps to prolong the latent phase.

6. Will multivitamin pills and herbal medicines help to delay the onset of symptomatic HIV infection?

Multivitamin supplementation is good but there is little evidence that specific nutritional supplements help if the person is on a good diet, while herbal remedies can have serious side effects and drug interactions with the antiretroviral medication.

Case study 3

A depressed patient with AIDS is referred to a HIV counsellor. She has a good knowledge of HIV infections and is aware of the importance of her symptoms. She is on antiretroviral treatment but has been diagnosed with lymphoma and is not responding well to chemotherapy.

1. What is HIV counselling?

Counselling is a method which uses education, communication and support to help a person manage their lives better, make decisions and find realistic ways to handle their problems. Counselling is more than just education.

2. Can someone who is not a health professional become a counsellor?

Yes. Many people from the community can be trained to become good counsellors.

3. What skills are needed by a counsellor?

They need to have a good knowledge of HIV infection and also be able to communicate well with people.

4. What is active listening?

Active listening notices body language and emotional reactions as well as words to understand what a person is trying to say. Active listening is the key to effective counselling.

5. What are commonly missed signs of depression?

A depressed mood, sadness, lack of interest in the world around them, sleep disturbances and suicidal thoughts. Depressed patients should be referred for assessment and possible treatment with antidepressants.

6. Is it worth treating a person with AIDS if their prognosis is poor?

Most definitely. Many of the symptoms of AIDS can be relieved and the quality of their lives improved during the last weeks and months. Patients should never be allowed to feel that they have been abandoned by the health carers.

Case study 4

A terminally ill man with AIDS is being cared for at home by his family. He has constant severe pain and the family is exhausted and can no longer manage.

1. Who should look after this patient?

It would be best if he could remain at home, but the family will need help. Failing this, it may be possible to move him to a hospice. Only as a last resort should he be admitted to hospital. Volunteer health workers could help with the many tasks needed in the home, such as cleaning and cooking. They can also help with washing and cleaning the patient.

2. Could the hospice advise on his home care?

Yes. Staff from the local hospice do home visits and are very experienced in the care of terminally ill patients.

3. What would be the best pain management for this man?

Usually analgesics for mild pain (e.g. paracetamol) and moderate pain (e.g. codeine) are tried first. However, this patient probably needs morphine for severe pain.

4. What is the preferred way of giving morphine?

By mouth every four hours. The dose of morphine is increased until the pain is controlled. The aim is to prevent pain and not to give morphine only when the pain is severe.

5. What is the common side effect of morphine?

Constipation. This can be controlled by adding fruit, bran and extra liquid to the diet. A laxative should also be given. Nausea and drowsiness may occur but they usually improve with time.

6. What is a memory box?

It is a box in which dying patients can put mementos, such as photographs, letters and cards, that can be given to their children when they are older. It enables terminally ill patients to leave something behind which will help their children remember them.

3

Preparation for antiretroviral treatment

Before you begin this unit, please take the corresponding test to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- List the indications for antiretroviral treatment.
- Refer a patient for antiretroviral treatment.
- Give the reasons for postponing antiretroviral treatment.
- State the risks of starting antiretroviral treatment too early or too late.
- Prepare a patient for antiretroviral treatment.
- Describe the first and second screening visit.
- Explain the role of lay counsellors.
- Describe 'treatment readiness'.

Indication for antiretroviral treatment

3-1 When should antiretroviral treatment be started?

Antiretroviral treatment (ART) is best started when a patient's immune function begins to decrease. This is indicated by either one or both of the following:

1. The clinical symptoms and signs
2. The CD4 count

Antiretrovirals should also be started in all pregnant or breastfeeding women to prevent mother to child transmission of the virus.

Antiretroviral treatment should preferably be started before a patient's immune system begins to fail.

3-2 Which clinical signs indicate that antiretroviral treatment should be started?

The 2013 South African treatment guidelines recommend that antiretroviral treatment should be

started when the patient reaches clinical stage 3 or 4 disease.

All pregnant and breastfeeding women and all patients with TB should start ART irrespective of their CD4 count.

Antiretroviral treatment should be started when stage 3 or 4 is reached.

3-3 What CD4 count is an indication to start antiretroviral treatment?

Antiretroviral treatment should be started when the CD4 count falls below 350 cells/µl, even if the clinical stage is still 1 or 2.. The aim of antiretroviral treatment is to prevent the CD4 count dropping further.

NOTE The World Health Organisation recommends antiretroviral treatment should be started in all patients with a CD4 count less than 500cells/µl.

3-4 Are both the clinical stage and the CD4 count equally important indicators for antiretroviral treatment?

Yes. Both the clinical stage of HIV infection and the CD4 count should be considered when deciding on whether to start antiretroviral treatment or not. Either the clinical stage of HIV infection (e.g. stage 3 or 4) or the CD4 count (e.g. below 350 cells/µl) may be used as an indication to start treatment. Therefore, treatment is indicated in a patient who is stage 2 but with a CD4 count below 350 cells/µl. Similarly, treatment should be started in all stage 4 patients even if their CD4 count is still above 350 cells/µl.

Both the clinical stage of HIV infection and the CD4 count are used as independent indicators for starting antiretroviral treatment.

NOTE A low CD4 count is the most common scenario for starting antiretroviral treatment.

3-5 Should patients be asked whether they are ready for antiretroviral treatment?

Yes. It is a major decision to start antiretroviral treatment as these patients will have to take drugs every day for the rest of their life. The patients must be fully counselled and given time to consider all the implications. Their opinion is very important and they must agree before treatment is started. They must understand the implications, the benefits and the side effects. Patients must be prepared and ready to start antiretroviral treatment. Treatment will fail if the patient is not ready and willing to start.

Patients must be fully informed and willing to start antiretroviral treatment.

3-6 What are the combined medical and personal criteria for preparing a patient for starting antiretroviral treatment?

Patients should have a CD4 count below 350 cells/μl or stage 3 or 4 disease plus a readiness and commitment to lifelong treatment. Therefore both medical and psychosocial factors are important in deciding when a patient should start antiretroviral treatment.

Both medical and personal factors must be considered before starting antiretroviral treatment.

Referral for anti-retroviral treatment

3-7 Who should refer a patient for antiretroviral treatment?

The nurse at the HIV clinic or general primary-care clinic, if an HIV clinic is not available. As the decision to start antiretroviral treatment is often complex, and as patient preparation is so important, this assessment should be done at a antiretroviral clinic if possible. All HIV clinics should know the criteria for patient referral. Patients should not be referred for antiretroviral treatment before the criteria are met.

3-8 How should patients be referred to the antiretroviral clinic?

Patients should be sent to the antiretroviral clinic with a full referral letter. A standardised referral letter is helpful. Send the latest CD4 count if available. An appointment should be made. The patient must be told the venue, date and time of the appointment. Keeping appointments is a good index of patient reliability.

Patients who meet the criteria for treatment should be referred to the antiretroviral clinic.

3-9 Who makes the final decision whether a patient should be given antiretroviral treatment?

The multidisciplinary team at the antiretroviral clinic. The team consists of the doctor, nurse,counsellor and community care worker. If possible a social worker, pharmacist, psychologist and dietician should also be part of the team.

All the important management decisions should be made by a multidisciplinary team.

Problems with starting antiretroviral treatment

3-10 What happens if the criteria for antiretroviral treatment are not met?

The patient is referred back to their local clinic with a letter providing the reasons why the patient has not been accepted for antiretroviral treatment. The local clinic should follow these patients and refer them again to the antiretroviral clinic when the criteria (stage 3 or 4 or CD4 count below

350 cells/μl have been met. Any psychosocial problems identified during screening should be addressed. Patients should be provided with counselling to encourage disclosure so that they can obtain social support.

3-11 Should psychosocial factors be used as exclusion criteria for antiretroviral treatment?

No. However, psychosocial considerations (emotional, family and community problems) are very important when a patient is being assessed for antiretroviral treatment. Antiretroviral treatment is likely to fail if there are major psychosocial problems. Therefore, provided antiretroviral treatment is not urgently required for clinical reasons, it may be postponed until the psychosocial problems have been addressed.

Psychosocial problems are useful in predicting whether treatment is likely to be successful or not.

3-12 What are the common causes for postponing antiretroviral treatment?

Antiretroviral treatment is postponed (deferred) if:

1. The patient does not meet the medical criteria (staging or CD4 count).
2. The patient is clinically well and not 'treatment ready', i.e. is not fully prepared for lifelong antiretroviral treatment.
3. The patient has a major psychosocial problem which needs to be addressed first.
4. The patient is unreliable and does not attend the clinic regularly.
5. The patient has an HIV-associated infection (e.g. tuberculosis) which should be treated first.

Treatment however should not be delayed if the patient has a CD4 count below 100 cells/μl, has Stage 4 disease, is pregnant or has drug-resistant TB. In these instances extra counseling support should occur during the first weeks of treatment.

3-13 What problems may result if treatment is started too early?

Starting too early when a patient is not treatment ready may lead to:

1. Unnecessary cost and inconvenience
2. Poor adherence to treatment
3. Drug resistance
4. Side effects

Poor adherence and drug resistance will decrease the chances of a good response to antiretroviral treatment when it is really needed.

3-14 What may happen if antiretroviral treatment is started too late?

Patients may die of the complications of HIV infection if antiretroviral treatment is started too late. Therefore, the correct timing of starting treatment is very important and is a balance between the risks of poor adherence, drug resistance and side effects if started too early, and the risk of

serious illness if started too late. If antiretroviral treatment is started too late (e.g. with a CD4 count below 50 cells/µl) the immune system may have been so badly damaged that full recovery is no longer possible.

The timing of starting antiretroviral treatment is a balance between the risks of starting too early and the dangers of starting too late.

3-15 How long does it take to assess and prepare a patient for antiretroviral treatment?

Usually two to four weeks. During this time the patient is prepared for the start of antiretroviral treatment.

It usually takes two to four weeks to prepare a patient for antiretroviral treatment.

3-16 Is starting antiretroviral treatment ever an emergency decision?

Starting antiretroviral treatment is never an emergency. But sometimes the indication to start may be urgent and treatment should not be unnecessarily delayed. Wherever possible, patients must be fully prepared before treatment is started and this always takes time. Preferably do not rush the decision or force patients who are well to start antiretroviral treatment before they are ready. Patients must show a commitment to take their medication correctly and follow instructions. However, in some cases the preparation may need to be as fast as possible, e.g. pregnant and breastfeeding women or patients with CD4 counts below 50cells/µl or stage 4 disease.

Starting antiretroviral treatment becomes urgent when the patient is demented or very weak and ill. In many of these cases the patient will die if treatment is delayed until they are fully prepared.

NOTE Patients with TB meningitis or Cryptococcal meningitis should start ART within 4-6 weeks after starting their treatment for TBM or CM. Staring ART earlier for these patients increases the risk of death due to immune reconstitution inflammatory syndrome (IRIS).

The decision to start antiretroviral treatment usually is not an emergency and must not be rushed.

3-17 What psychosocial factors should be considered before starting antiretroviral treatment?

1. Patients must show that they are both motivated and reliable. Otherwise adherence to treatment will be poor and they will not attend clinic regularly.
2. They must accept their HIV status and have a good understanding of HIV infection and antiretroviral treatment.
3. There should be no unmanaged alcohol or drug abuse.

4. They should not have untreated active depression.
5. They are strongly advised to disclose their status to at least one person.
6. They must have access to an antiretroviral centre and HIV clinic.
7. They should have the support of their partner, a friend or family member.

Preparing for antiretroviral treatment

3-18 Why is it important to prepare the patient before starting antiretroviral treatment?

If the treatment is begun before the patient is ready to start treatment, there will almost certainly be poor adherence. The success or failure of antiretroviral treatment often depends on whether the patients have been well prepared or not. One of the main reasons for treatment failure and poor co-operation from patients is inadequate preparation.

Inadequate preparation is an important cause of poor co-operation and treatment failure.

3-19 Why is excellent adherence so important?

It is very important that HIV patients take their correct medication on time every day. Poor adherence to taking medicine correctly leads to HIV resistance to one or more of the antiretroviral drugs being used. This reduces the drug options later in the course of the illness. Taking the first regimen of antiretroviral drugs correctly is the best chance the patient has to be healthy and well for many years.

Excellent drug adherence is extremely important for the successful management of AIDS.

3-20 What are the aims of preparing a patient for antiretroviral treatment?

1. The patient must have a good understanding of HIV infection.
2. The names, dosing and timing of the antiretroviral agents must be learned. Patients should be taught to recognise their different drugs.
3. The risks and symptoms of side effects must be known.
4. The importance of excellent adherence must be understood and accepted.
5. Disclosure to a partner, close family and friends is needed.
6. Social support is essential.
7. The patient must learn a healthy lifestyle.
8. The patient must accept regular follow-up care.

3-21 What issues should be discussed with patients before starting antiretroviral treatment?

1. The purpose of giving antiretroviral treatment is to give them a longer, healthier life.
2. Antiretroviral treatment cannot cure HIV infection.
3. They will still be infectious and be able to pass on HIV even while on treatment.

4. Treatment is lifelong.
5. The drugs must be taken correctly every day for the treatment to be effective.
6. They will need regular blood tests and clinical check-ups.
7. Side effects to the treatment may occur.
8. They should find a treatment supporter.
9. They need to consider the effects of daily treatment on their lifestyle.

Screening visits

3-22 What visits to the antiretroviral clinic are needed before treatment is started?

Usually two treatment readiness visits are needed, followed by the final visit when treatment is started.

1. The screening visit is usually the patient's first contact with the antiretroviral clinic. The patient should receive a clinical assessment at this visit, have baseline bloods taken and receive information on the pre-treatment counselling programme.
2. The second visit may be used to prepare the patient for treatment and assess whether the patient is ready for lifelong ART.
3. At the third visit, a final decision is made and, if the patient is ready, treatment is started.

Usually two visits are needed to fully assess a patient for antiretroviral treatment.

3-23 What should be done at the first screening visit?

1. A doctor or ART trained nurse should confirm that the clinical or immunological selection criteria for anti¬retroviral treatment have been met. This requires a general medical screening examination.
2. Identify any psychosocial problems.
3. Make sure that tuberculosis has been excluded. This may require a chest X-ray and sputum tests.
4. Diagnose and treat any HIV-associated infection.
5. The patient's information record must be completed.
6. The patient must meet or be referred to the counselling team for group education and/or individual counselling.
7. Supply a 28-day supply of co-trimoxazole tablets.
8. Give the patient an appointment for the next visit (usually the second visit in two weeks' time).
9. Arrange a home visit, if possible.

3-24 What general medical screening examination is necessary?

1. Take a medical history.
2. Obtain details of the patient's social circumstances.
3. Find out whether the patient has disclosed his/her HIV status to their partner and close family and friends.
4. Ask what family and community support is available.
5. Perform a full general physical examination.

3-25 What medical history is needed?

1. Any symptoms or signs of HIV and associated infections.
2. Recent weight loss.
3. Recent hospital admissions.
4. Recent history of TB.
5. Any sexually transmitted diseases.
6. Current medication or allergies.

3-26 What social history is important?

1. Age.
2. Find out whether the patient understands what AIDS is and what the implications of the diagnosis are.
3. Family structure and home environment.
4. Sexual relationships and condom use.
5. Whether women are on reliable contraception and if pregnancies are planned.
6. Employment and family income.
7. Available support.
8. Disclosure.
9. Alcohol or drug abuse.
10. Severe emotional problems, e.g. depression.

3-27 What physical examination is required?

1. Full general physical condition.
2. Any signs of weight loss.
3. Clinical signs of HIV and associated infections.
4. Assess the clinical stage of the patient.

3-28 Who should prepare a patient for antiretroviral treatment?

This is best done by the multidisciplinary staff of the health centre where antiretroviral treatment is started. The doctor, nurse, counsellor, and pharmacist all play an important role in preparing a patient for antiretroviral treatment. Sometimes patients are referred for special treatment readiness classes.

Patients need to attend a treatment readiness programme.

3-29 What are the steps in preparing a patient for antiretroviral treatment?

1. Education
2. Counselling

3-30 What education is needed?

The patient needs to:

1. Understand what HIV infection is
2. Understand what antiretroviral treatment is
3. Know the names and appearance of the antiretroviral drugs to be used
4. Know the dose and how to take these drugs correctly
5. Know the symptoms and signs of the side effects
6. Know about the common HIV-associated infections
7. Know that a good diet and a positive lifestyle are important

The patient needs to understand antiretroviral treatment ('patients must know their meds'). It is particularly important that the patient accepts that excellent adherence is essential and understands that resistance is dangerous, and that failure of treatment and resistance are usually due to poor

adherence.Patients need to know about the drugs they will be taking.

3-31 How is education provided?

1. During individual counselling sessions
2. In group education classes
3. With pamphlets on HIV infection and antiretroviral treatment
4. Posters and videos are helpful
5. A treatment chart illustrating the drugs, timing of doses and possible side effects

3-32 What counselling is needed?

The patient may need help in accepting their HIV status and the importance of antiretroviral treatment. They may also have difficulty disclosing their HIV status and finding someone who can support them. All patients preparing for antiretroviral treatment should be encouraged to join a support group. Patients need an opportunity to talk about their fears and concerns. Counselling empowers patients to make the best decisions for themselves and take control of their lives. It helps them understand, accept and make choices.

Disclosure and support are needed for successful treatment.

3-33 Why is co-trimoxazole prophylaxis started?

Co-trimoxazole provides protection against pneumocystis pneumonia, toxoplasmosis, many bacterial infections and some causes of chronic diarrhoea.

3-34 How is co-trimoxazole prophylaxis given?

Two single-strength tablets daily (i.e. 80/400 mg). The commonest side effect is a maculopapular rash. Continue the co-trimoxazole if the rash is mild. Stop immediately if the rash is severe or blistering, the mucous membranes are involved, or the patient becomes ill with fever.

NOTE Dapsone can be used if patients have severe side effects to co-trimoxazole.

3-35 Can the degree of drug adherence be assessed before starting antiretroviral treatment?

Yes, as patients who are not adherent to prophylactic co-trimoxazole will probably not adhere to antiretroviral treatment. Patients should bring their unused tablets to each clinic visit. These should be counted to assess adherence. If all the tablets needed have not been taken, the patient should be counselled to find out why adherence is poor. The advantages and importance of excellent adherence must again be stressed.

Adherence to co-trimoxazole is a good indicator of adherence to antiretroviral treatment.

3-36 Is a home visit always needed?

A home visit is very helpful to assess the home circumstances and family support, and whether the patient has provided the correct contact and social details. A reliable home address is essential and a telephone contact

number is useful. A home visit also helps to determine whether the patient has disclosed his/her HIV status.

3-37 Who does the home visit?

This is usually done by a lay counsellor who has taken on the role of community care worker or home based carer.

3-38 What are the benefits of lay counsellors?

Some lay counsellors are on antiretroviral treatment themselves. They have a personal understanding of what it means to have HIV infection and successfully adhere to treatment. As a result, these lay counsellors are good role models for patients starting antiretroviral treatment.

Lay counsellors undergo careful training which provides them with the knowledge and skills to function in their new role as counsellors and educators. Without lay counsellors, most antiretroviral clinics would not be able to function. They are essential members of the treatment team as they know the community well, usually speak the patients' home language and help to maintain close contact between patients and the clinic.

Lay counsellors promote a healthy lifestyle and often follow up the patient once antiretroviral treatment is started. Tracing patients that fail to collect their medicines regularly or miss a clinic appointment is an important function.

Lay counsellors are valuable members of the treatment team.

3-39 Should patients have their own counsellor?

A personal counsellor is a great advantage if it is possible to have one. Often the success of antiretroviral treatment depends on the help and support of a lay counsellor. The counsellor should develop a special, caring relationship with the patient. They can perform the home visit, meet the patient at each clinic visit and act as the contact between the patient and the clinic team.

It is a great advantage if each patient can have a personal counsellor.

3-40 What should be done at the second clinic visit?

The second visit is usually arranged for two weeks after the first visit. During this time the patient has had time to consider the implications of antiretroviral treatment. The following should be done at the second assessment visit:

1. If the patient is unwell, a clinical assessment should be repeated.
2. A second group education and information session is provided.
3. The patient is again counselled about the importance of excellent adherence.

4. The co-trimoxazole tablets are counted (pill count) to assess adherence.
5. Blood results are checked and tests are repeated if necessary.

The second visit is followed by a multidisciplinary team discussion.

3-41 What is the multidisciplinary team discussion?

Following the second visit the patient must be assessed for readiness for antiretroviral treatment by a multidisciplinary team. This is done by the whole treatment team and not just one person. All the available information must be ready for the discussion (clinical assessment, results of the two educational and counselling sessions and a home visit report if possible). This is the final check that the patient is fully prepared for treatment.

Patients who are ready for treatment should be given an appointment for their antiretroviral treatment commencement visit which will be two weeks later.

3-42 What is a treatment plan?

The treatment plan is the formal guide to the patient's future management. Each patient must be fully aware of their own treatment plan. Usually the treatment plan is given to each patient as a printed form.

It is essential that each patient has a clearly understood treatment plan.

3-43 When are patients 'treatment ready'?

1. They show a willingness for treatment.
2. They demonstrate insight into their illness.
3. They accept that lifetime treatment is required.
4. They understand the possible side effects of antiretroviral treatment.
5. They recognise the importance of excellent daily adherence.
6. They have preferably disclosed to a family member or friend who can support them.
7. They are able to attend the clinic regularly.
8. They must know the names and recognise which drugs are to be taken.
9. They must know the symptoms and signs of common side effects.

If patients are not treatment ready yet and are clinically well, the start of antiretroviral treatment should be postponed until they are ready and all the requirements have been met.

3-44 What baseline blood tests are needed?

The baseline CD4 count has usually been done before the patient is referred for treatment consideration and, therefore, need not be repeated. If the CD4 count was not measured, this should be done at the screening visit.

Special blood tests depending on the likely side effects of the specific drugs being used:

1. Haemoglobin level (Hb) and differential white count (or full

blood count) if AZT (zidovudine) is used
2. Serum ALT (alanine aminotransferase) if nevirapine is used
3. Fasting serum glucose, cholesterol and triglyceride if 'PIs' such as lopinavir/ritonavir are used
4. Creatinine for creatinine clearance if tenofovir (TDF) is being used

NOTE To calculate creatinine clearance: (140 – age in years) × weight in kg / serum creatinine concentration (× 0.85 in women)

Other routine baseline blood tests:

1. RPR to check for syphilis if not done by referring clinic.
2. Cryptococcal latex agglutination test (CLAT) should be done on all patients with a CD4 below100cells/µl to identify patients who require cryptococcal meningitis prophylaxis with fluconazole.

NOTE Patients with a positive CLAT and no symptoms of meningitis should be treated with 800mg fluconazole by mouth daily for 2 weeks, then 400mg daily by mouth for 8 weeks, then 200mg per day until the CD4 count is below 200cells/µl for at least 6 months.

3-45 What should be done when patients are ready for treatment?

They should be asked to continue their co-trimoxazole prophylaxis and be given an appointment for their next visit in two weeks when antiretroviral treatment will begin.

Once it is agreed that antiretroviral treatment should be started, the drug regime and doses must be decided on and the drugs should be ordered from the pharmacy. It is helpful to have a system which maintains a close check on medication collected.

Case study 1

A patient who has had symptomatic HIV infection for the past year is referred to an antiretroviral clinic for treatment. Her CD4 count is 150 cells/µl and she has been clinically graded as stage 4. She is unhappy about starting treatment as she does not want to disclose her HIV status to her partner and family. She has a chronic cough.

1. Does her immunological status meet the criteria for antiretroviral treatment?

Yes, as her CD4 count is below 350 cells/µl. This indicates that her immune function is depressed and she is at high risk of contracting an opportunistic infection unless she receives antiretroviral treatment.

2. Is stage 4 disease a criteria for treatment?

Yes. Stage 4 HIV infection (i.e. AIDS), with or without a low CD4 count, is a criteria for treatment. She therefore meets both the immunological and clinical criteria for treatment.

3. Do you think she should start on antiretroviral treatment?

No, as she has psychosocial problems. She is not happy about starting treatment and has not disclosed her status to either her partner or family.

4. Should psychosocial factors exclude her from treatment?

No, but she should be counselled and be helped to become 'treatment ready'. Without disclosure, support and a firm commitment to daily medication, she will almost certainly not succeed with antiretroviral treatment.

5. Would tuberculosis result in postponement of treatment?

Tuberculosis treatment should be started before beginning antiretroviral treatment.

Case study 2

A patient who meets both the medical and psychosocial criteria for treatment attends his first screening visit. He is very keen and wants treatment to start immediately.

1. Should he be offered treatment immediately as he wants to start straight away?

No. It is always important to make sure that the patient is well prepared before starting treatment. Starting antiretroviral treatment is not an emergency.

2. What should be done at the first screening visit?

A careful history should be taken and a full physical examination done to confirm that all the criteria for treatment have been met. Counselling and education sessions must be arranged and co-trimoxazole started.

3. Who should provide the counselling and education?

All the members of the multidisciplinary team play a role. Individual counselling is important. Pamphlets, videos and posters are helpful. A group education course may be available.

4. What must the patient learn about antiretroviral treatment?

He must know what drugs are to be taken, the dose and timing of treatment, and the side effects. He must 'know his drugs'. The importance of excellent adherence must be stressed at every meeting. He must be aware of the risks and advantages of treatment.

5. Why should he start co-trimoxazole?

It prevents many of the infections associated with HIV. It is also a measure of the patient's willingness to take regular medication. A 'pill count' assesses whether all doses have been taken. Taking all his co-trimoxazole tablets as prescribed suggests he will also adhere to antiretroviral treatment.

6. What is the most important lesson to learn about taking antiretroviral drugs?

For successful treatment drug adherence must be excellent.

Case study 3

After the first screening appointment a home visit is arranged. This is done by a community care worker. The community care worker discovers that the patient is drinking heavily over weekends.

1. What is the aim of the home visit?

To help assess the home circumstances, especially disclosure and support. It is also important to confirm the home address and contact phone number.

2. Should the home visit not be done by a professional counsellor?

Usually there are not enough professional counsellors to do all the home visits. Therefore community care workers or home based carers often perform this function. They are well trained and employed by the clinic.

3. What are the advantages of a community care worker?

They sometimes are HIV positive and well managed on antiretroviral treatment. As a result they have personal experience of the problems of HIV management. They come from the local community and have a good understanding of the social circumstances. Usually the community care worker can speak the patient's home language. The community care worker is a good role model for the patient starting antiretroviral treatment.

4. Would alcohol abuse be a contraindication for starting antiretroviral treatment?

Yes, if uncontrolled. So would untreated active depression or drug abuse. These problems would need to be successfully managed before treatment could start. Discovering this problem stresses the importance of a home visit.

5. What other support can a lay counsellor provide?

They help with counselling and education. Lay counsellors keep close contact between patients and the clinic. They help promote a healthy lifestyle with a positive outlook.

Case study 4

A patient attends the screening visit. After she is seen by the doctor, blood samples are taken. She is assessed for treatment readiness and told to return to the clinic for treatment readiness classes.

1. What blood tests are done at the screening visit?

A CD4 count is done if this has not already been checked. Additional blood tests are done depending on the drugs to be used. A full blood count for AZT, serum ALT for nevirapine and fasting glucose, cholesterol and triglyceride for lopinavir/ritonavir.

2. When are patients 'treatment ready'?

When they are willing to accept that treatment is for life and excellent adherence is the key to successful

treatment. They must understand how to take their medication correctly and know what side effects to expect. They should also be able to attend clinic regularly, have preferably disclosed their HIV status and have good home support.

3. Who decides when a patient is ready to start treatment?

The multidisciplinary team. The decision should not be taken by the doctor alone.

4

Antiretroviral drugs

Before you begin this unit, please take the corresponding test to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- List the goals of antiretroviral treatment.
- Describe the three classes of antiretroviral drugs commonly used.
- Describe the actions of antiretroviral drugs.
- Define multi-drug treatment of HIV.
- Give the advantages of standardised regimens.
- List the first- and second-line drug combinations.
- Describe how antiretroviral drugs should be taken.
- Recognise common and serious side effects of antiretroviral drugs.

Introduction to anti-retroviral treatment

4-1 What is antiretroviral treatment?

Antiretroviral treatment (ART) is the use of drugs (i.e. medicines) to treat patients with HIV infection.

NOTE In 1996 Dr David Ho of New York presented the results of a landmark study showing that multi-drug antiretroviral treatment was successful in stopping viral replication and controlling the immune damage of HIV.

4-2 How does antiretroviral treatment work?

Antiretroviral drugs prevent HIV from multiplying (making copies of itself) in the CD4 lymphocytes. This reduces the number of viruses in the body and, thereby, allows the damaged immune system to recover. Antiretroviral treatment results in an improvement of the clinical disease.

Antiretroviral treatment stops HIV from multiplying in the body.

4-3 What are the goals of antiretroviral treatment?

The goals are to:

1. Prevent the multiplication (replication) of HIV and, thereby, suppress the viral load and keep it suppressed.
2. Prevent the further destruction of CD4 cells and allow the immune function to recover.
3. Improve the quality of life and general health by decreasing the

clinical signs and symptoms of HIV infection.
4. Reduce the occurrence of HIV-associated infections.
5. Reduce the risk of death due to AIDS.
6. Do this with minimal antiretroviral side-effects.

The main goals of antiretroviral treatment are to improve the quality of life and reduce mortality due to AIDS.

4-4 At what sites in the CD4 lymphocytes do antiretroviral drugs act?

1. At the stage where the virus enters the cell.
2. At the stage where the virus gives instructions to produce new viruses.
3. At the stage where new viruses are manufactured and released into the body.

Classes of antiretroviral drugs

4-5 What are the classes of antiretroviral drugs?

The most commonly used drugs fall into one of three classes:

1. Nucleoside reverse transcriptase inhibitors and nucleotide reverse transcriptase inhibitors, are also known as 'nucs' (pronounced as 'nukes'). They act at the stage where the virus infecting the CD4 lymphocyte gives instructions to these cells to produce new viruses.
2. Non-nucleoside reverse transcriptase inhibitors are commonly called 'non-nucs'. They also act at the stage where the virus gives instructions to the CD4 cells to produce new viruses but the method of action is different from the 'nucs'.
3. Protease inhibitors ('PIs'). They act at the final stage where the CD4 cell manufactures new viruses.

NOTE Nucleoside reverse transcriptase inhibitors (NRTIs) and nucleotide reverse transcriptase inhibitors (NtRTIs) are also known as nucleoside and nucleotide reverse transcriptase antagonists. Two new classes of antiretrovirals (intergrase inhibitors and entry inhibitors) have also been available in recent years. NRTIs were the first group of antiretroviral drugs available.

4-6 What are common examples of 'nucs'?

1. TDF (tenofovir)
2. 3TC (lamivudine)
3. AZT (zidovudine)
4. FTC (emtricitabine)
5. ABC (abacavir)
6. d4T (stavudine)
7. ddI (didanosine)

These are the generic (common) names of the drugs. For each generic drug there are one or more different trade names for the same drug manufactured by different companies. This makes it difficult to remember all the trade names. Therefore, it is best to remember the generic names and only the commonly used trade names of the frequently used antiretroviral drugs. If possible, use the generic names rather than the trade names.

NOTE NRTIs mimic (look like) natural nucleosides (DNA building blocks, e.g. thymidine) and thereby block the function of the reverse transcriptase enzyme. They act as false building blocks for HIV DNA and prevent the HIV instructions being inserted into the DNA of the CD4 cells.

4-7 Can different 'nucs' be used together?

'Nucs' are generally used in pairs, e.g. TDF and FTC or AZT and 3TC. However, AZT and d4T should not be used together as they compete with each other. AZT and 3TC can be combined as Combivir. TDF is usually given with 3TC or FTC.

AZT and d4T should never be used together as they compete with one another.

4-8 What are common trade names for the 'nucs'?

Common 'nucs' are:

1. AZT is sold as Retrovir.
2. 3TC is simply called 3TC.
3. d4T is sold as Zerit.
4. ddl is sold as Videx.
5. TDF is sold as Viread.

NOTE TDF together with FTC is sold as Truvada.

4-9 What are examples of 'non-nucs'?

Common 'non-nucs' are:

1. Nevirapine
2. Efavirenz

'Non-nucs' are particularly powerful inhibitors of HIV multiplication. However, HIV rapidly becomes resistant to 'non-nucs' if they are used alone. Therefore, they are usually used with a pair of 'nucs'.

NOTE NRTIs directly inhibit the reverse transcriptase enzyme by binding to it and thereby prevent the formation of DNA containing the HIV genetic code in the CD4 lymphocytes.

4-10 What are common trade names for the 'non-nucs'?

- Nevirapine is called Viramune.
- Efavirenz is called Stocrin.

4-11 What are examples of 'PIs'?

1. Ritonavir
2. Lopinavir
3. Atazanavir

The common trade name for ritonavir is Norvir. Sometimes two 'PIs' (protease inhibitors) are put together in a single preparation such as Aluvia (a trade name for lopinavir combined with ritonavir). Using two 'PIs' together allow a lower dose of both with fewer side effects. Atazanavir is also always used in combination with ritonavir, but they are given as separate tablets.

There are a large number of other 'PIs'. They are easy to recognise as their generic names all end in 'avir' such as ritonavir.

NOTE A low dose of ritonavir is used to boost the effect of lopinavir.

4-12 Can antiretroviral drugs be taken by mouth?

Yes. The common antiretroviral drugs in all classes can be taken by mouth.

It is very important that all antiretroviral drugs are taken at the same time every day.

All antiretroviral drugs must be taken by mouth at the same time every day.

4-13 Should a number of antiretroviral drugs be used together?

Yes. With antiretroviral treatment it is essential to use a number of drugs together. This is called multi-drug treatment. It is important to use multi-drug treatment as it is more effective and also reduces the chance of the HIV becoming resistant to the drugs. The same advantages of multi-drug therapy apply to the treatment of TB. Except for the prevention of mother-to-child transmission and post-exposure prophylaxis, single or double drug treatment of HIV infection should never be used.

Multi-drug treatment should be used to treat HIV.

NOTE Multi-drug treatment of HIV infection in 1995 showed dramatic results following earlier disappointing results with single drug treatment.

4-14 What is HAART?

Highly active antiretroviral treatment (HAART) is another name for antiretroviral treatment (ART). It is the use of multiple drugs to treat HIV infection. Three or more drugs are always used together for antiretroviral treatment.

Three or more antiretroviral drugs are always used to provide antiretroviral treatment.

NOTE Sometimes one drug (monotreatment) or two drugs (dual treatment) have been used in short-course prophylactic treatment to prevent the transmission of HIV from mother to child during pregnancy and delivery. One or two drugs are only appropriate in HIV prophylaxis.

4-15 Can antiretroviral treatment cure HIV infection?

Unfortunately not. However, antiretroviral treatment can dramatically improve the symptoms and clinical signs of HIV infection and allow the patient to remain healthy for many years. Antiretroviral treatment is the most important advance in the management of HIV infection. Antiretroviral treatment can change the outcome of HIV infection from a rapidly fatal disease into a manageable chronic illness.

Antiretroviral treatment is the most important advance in the management of HIV infection and has changed the course from a rapidly fatal disease into a manageable chronic illness.

NOTE In November 2003 the South African government agreed to the widespread introduction of antiretroviral treatment in the management of patients with HIV infection.

Standardised regimens for antiretroviral treatment

4-16 What is a standardised regimen for treating HIV infection?

The choice of which antiretroviral drugs to use can be based on either an individualised or a standardised approach. Initially an individualised approach was used where the most appropriate drugs were chosen to meet the needs of each patient. More recently a standardised approach has been used where all patients are started on the same combination, as is done with TB treatment.

4-17 What are the advantages of using a standardised regimen?

1. The standardised approach is safer, easier and simpler.
2. It is also affordable and effective.
3. Both healthcare workers and patients can learn how to use these drugs correctly and which side effects to be aware of. The education and training of healthcare workers and patients are much easier.
4. It limits the number of drugs that are used and makes it possible to monitor patterns of drug use and resistance. Monitoring for side effects is simplified.
5. It is easier to buy and distribute a limited range of drugs.
6. Fixed doses are used in the standardised approach.

The standardised approach to antiretroviral drugs is preferred.

A standardised regimen consists of a specific combination of antiretroviral drugs where the risk of drug interactions and side effects are low. The drug combination should target at least two sites in the life cycle of HIV (i.e. important stages in the viral replication).

4-18 What are the disadvantages of an individualised approach?

Using combinations of antiretroviral drugs is very complicated as each combination has its own risk of drug interactions. Some drugs counteract each other (block the function of the other drug). Other drug combinations have a high risk of serious side effects. Therefore, a wide knowledge and experience of these drugs is essential if the individual approach is to be used. This ability is usually only available at antiretroviral clinics where particularly difficult management problems are referred.

4-19 What is a first-line combination?

This is the combination of drugs which is routinely used when patients first start antiretroviral treatment.

4-20 What is the first-line combination commonly used in South Africa?

When treating adults with HIV infection in South Africa, the first-line combination is usually two 'nucs' together with a 'non-nuc'.

The 2013 South African guidelines recommend the combination of TDF plus 3TC or FTC with efavirenz as first line treatment. Unless contraindicated, all patients, including pregnant women, should be started on this regimen which should preferably be prescribed as a once daily fixed dose combination tablet. AZT can be used if there are contraindications to TDF and nevirapine can be prescribed if efavirenz is contraindicated. Some old regimes still use d4T instead of TDF.

NOTE Sometimes TDF is combined with FTC and Efavirenz. This combination is commonly known as Atripla or Odimune.

In South Africa antiretroviral treatment is usually started with TDF, FTC and efavirenz in a single fixed dose combination tablet taken once daily in the evening.

This combination is chosen for its effectiveness and availability, few serious side effects and low cost.

4-21 What is a second-line combination?

Patients who fail to respond to the first-line combination, despite good adherence, are changed to a second-line combination of antiretroviral drugs.

NOTE Unfortunately there is no standardised third-line combination of drugs available in the public sector in South Africa. This will change when new drugs are made available in the future.

4-22 What common second-line combination is used in South Africa?

Usually two 'nucs' plus a combination of two 'PIs'. The common second-line combination in South Africa is AZT plus 3TC plus ritonavir and lopinavir together. TDF can be used instead of AZT if the failed first-line combination included AZTor d4t

The previous second-line combination of AZT, ddI and Aluvia is sometimes still used.

Therefore both the first- and second-line combinations include two 'nucs'. However, only the first-line combination includes a 'non-nuc' while only the second-line combination includes 'PIs'.

In South Africa the new second-line combination is AZT plus 3TC plus ritonavir and lopinavir together.

4-23 When are other combinations of antiretroviral drugs used?

Sometimes changes to the first- or second-line combinations are made when there are serious side effects to only one drug in a standardised regimen e.g.

1. Patients who experience severe psychological side effects to

efavirenz may be switched to nevirapine
2. Patients who are intolerant to lopinavir and ritonavir (i.e. who have severe diarrhoea over a number of weeks) may be switched to atazanavir and ritonavir.
3. Patients who are on the old first line regimen of d4t, 3TC and efavirenz or nevirapine may be changed to a fixed dose combination tablet of TDF, FTC and efavirenz if they have side effects due to d4t (lipoatrophy) or at at high risk of developing side effects (high BMI or pregnant)

These changes (swaps) should only be made by an experienced clinician at an antiretroviral clinic and care should be taken to ensure that the patient has a suppressed viral load at the time of the one drug switch. Using individualised combinations reduces the future options of treatment.

NOTE Patients who have failed to respond to both first- and second-line combinations, despite good adherence, may be offered 'salvage treatment' with new drugs.

Antiretroviral medication

4-24 What are the practical implications of taking antiretroviral treatment?

The following questions must be considered:

1. Which medications are taken?
2. How many tablets or capsules are taken at a time?
3. When and how often is the medication taken?
4. Should the medication be taken with or without food?
5. Can all the drugs be taken together at the same time?

4-25 How should tenofovir be taken?

TDF (generic name tenofovir) is a 'nuc' (trade name is Viread). One TDF 300 mg tablet is taken daily with or without food. TDF is usually taken at night without food. TDF may cause renal impairment, noted by an increase in serum creatinine concentration in the first few months of treatment.

Some patients on an older regime may still receive d4T (generic name stavudine). d4T is also a 'nuc' (trade name is Zerit). One 30 mg capsule is taken twice a day (12-hourly). Capsules can be taken with or without food. However, taking d4T with food reduces nausea. More recent guidelines do not include d4T.

NOTE Initially d4T may be well tolerated but in the long term 20% of patients will have side effects. These may include serious complications such as peripheral neuropathy, pancreatitis, hepatitis, lipodystrophy and lactic acidosis due to mitochondrial DNA depletion. The risk of these side effects is particularly high with d4T, and further increased if d4T is taken together with ddI or if the patient is a woman, obese or pregnant.

d4T must not be given with ddI.

4-26 How should 3TC be taken?

3TC is also a 'nuc' (generic name is lamivudine while trade name is also 3TC). One 150 mg tablet is taken twice a day (12-hourly) with or without food. However, 300 mg 3TC may be taken as a once-daily dose. 3TC is well tolerated and has very few side effects. Mild nausea, headache and diarrhoea may occur.

3TC is well tolerated with few side effects.

4-27 How should AZT be taken?

AZT (generic name zidovudine) is a 'nuc' (trade name is Retrovir). One 300 mg tablet is taken twice daily (12-hourly). Tablets can be taken with or without food. However, nausea may be less if taken with food. AZT has many short term minor side effects such as fatigue, nausea and vomiting, headache, muscle pains and altered taste. These are common at the start of treatment and are worse with higher doses. However, they become less after a few weeks. AZT may also discolour the nails.

The most important side effect of AZT is anaemia. This usually occurs in the first few months of treatment.

AZT may cause anaemia.

NOTE Serious complications of AZT are anaemia, neutropenia and lactic acidosis.

4-28 How should abacvir be taken?

ABC (generic name abacvir) is also a 'nuc' (trade name is Viagen). ABC 300mg (1 tablet) should be taken every 12 hours. ABC is usually used if a patient cannot take TDF, AZT or d4T. ABC is well-tolerated though there is a small risk of a severe initial hypersensitivity reaction.

NOTE Up to 3% of people taking ABC will have an initial reaction which can be severe and even fatal if treatment is not stopped.

NOTE ddI is another 'nuc' with the generic name didanosine and trade name Videx. Very little ddI is still being used in South Africa. Serious side effects of ddI include pancreatitis, peripheral neuropathy and lactic acidosis due to interference with mitochondrial metabolism.

4-29 How should nevirapine be taken?

Nevirapine is a 'non-nuc'. One nevirapine 200 mg tablet (trade name is Viramune) is taken at night to start with. After 14 days the dosage is increased to one tablet twice daily (12-hourly). If there is a mild rash or raised liver enzymes, do not increase the dose to twice a day until the liver enzymes have dropped and the rash has cleared.

A mild rash is common, usually during the first six weeks of treatment. A severe rash may also occur with nevirapine. The drugs must be stopped immediately if a severe rash appears.

NOTE Serious complications of nevirapine include blistering rash with mucosal

involvement, hepatitis and fever due to a hypersensitivity reaction.

Nevirapine may cause early, serious side effects.

4-30 How should efavirenz be taken?

Efavirenz is also a 'non-nuc' and is very similar to nevirapine.

One efavirenz 600 mg capsule (trade name Stocrin) is taken at night. Efavirenz has the advantage of the patient only needing a single dose a day.

A rash may occur. However this side effect is less common and not as severe as with nevirapine. Efavirenz commonly causes mild emotional symptoms for the first few weeks (mood changes, abnormal dreams, insomnia and dizziness). These are reduced if efavirenz is taken on an empty stomach in the evening. When side effects have cleared efavirenz should be taken with meals.

NOTE The absorption of efavirenz is greater if it is taken with meals. This may make side effects worse during the first weeks of treatment.

4-31 Who should not take efavirenz?

Until recently efavirenz was avoided during the first trimester of pregnancy, as it was thought to cause fetal abnormalities (birth defects). Recent data has shown no increase in fetal abnormalities with efavirenz and guidelines now allow the use of efavirenz throughout pregnancy.

Efavirenz is now thought to be safe in a woman who is at risk of falling pregnant.

4-32 How should 'PIs' be taken?

Usually lopinavir 400 mg and ritonavir 100 mg (LPV/r) are taken in combination as Aluvia.Two tablets of Aluvia are taken twice a day (12-hourly) with or without food. Nausea and diarrhoea are common for the first few weeks. These side effects can be reduced if the drug is taken with food. Due to drug interactions, the dosages of many drugs have to be altered if they are used together with lopinavir and ritonavir.

Atazanavir 300mg is usually taken with ritonavir 100mg, both once a day. Atazanavir is usually better tolerated than lopinavir. Patients may present with jaundice, due to an increase in unconjugated bilirubin. Liver functions will be normal. This jaundice is harmless and the atazanavir can be continued.

NOTE Protease inhibitors may cause lipodystrophy with abnormal fat distribution. Lipodystrophy may be associated with insulin resistance and hyperlipidaemia. Protease inhibitors may also affect the metabolism and breakdown of many drugs (ritonavir inhibits cytochrome P450 and thereby increases the blood level of lopinavir and a wide range of other drugs). A small dose of ritonavir therefore boosts the effect of lopinavir.

The dose of lopinavir/ritonavir must be increased if used with efavirenz or rifampicin. Expert advice should be

asked for. Atazanavir/ritonavir cannot be used with rifampicin.

4-33 Which antiretroviral drugs should not be taken with a meal?

It is important that ddI is taken on an empty stomach as food decreases the absorption of the drug. In addition, the side effects of efavirenz are less if the drug is taken on an empty stomach in the evenings. Therefore it is best if efavirenz is taken without food for the first few weeks. However, most other antiretroviral drugs can be taken once a day with meals.

Only ddI must be taken on an empty stomach.

If the previous second-line combination is used, AZT and lopinavir/ritonavir are best taken with meals, but ddI must be taken on an empty stomach. Take ddI at least an hour before or two hours after a meal.

It is important to know which drugs should be taken with meals and which drugs must be taken on an empty stomach.

Table 4-1: *Details of antiretroviral drugs*

Drug	Generic	Trade	Dose	Frequency[#]
TDF	tenofovir	Viread	300 mg	Daily
AZT	zidovudine	Retrovir	300 mg	Twice daily
3TC	lamivudine	3TC	300 mg	Daily
3TC**	lamivudine	3TC	150 mg	Twice daily
ABC	abacavir	Viagen	300 mg	Twice daily
d4T	stavudine	Zerit	30 mg	Twice daily
ddI	didanosine	Videx	400 mg	Daily
NVP	nevirapine	Viramune	200 mg	Twice daily*
EFV***	efavirenz	Stocrin	600 mg	Daily
LPV/r	lopinavir/ ritonavir	Aluvia	400 mg/100 mg	Twice daily
Atazanavir/ ritonavir	atazanavir/ ritonavir	Reyataz/Novir	300 mg/100 mg	Daily

[#] Twice daily doses are best taken 12 hours apart e.g. 7 am and 7 pm.
* Only one tablet of nevirapine daily at night for the first two weeks of treatment
** 3TC is taken as a 300 mg dose daily with EFV and TDF but as a 150 mg dose twice daily with AZT and NVP.
*** Efavirenz is best taken on an empty stomach for the first few weeks.

4-34 Which drugs must be kept cool?

The antiretroviral drugs currently used do not need to be kept in a fridge.

Side effects of antiretroviral drugs

4-35 Do all antiretroviral drugs have side effects?

Side effects to antiretroviral drugs are common and usually mild, but they can sometimes be severe. Remember that drugs used to treat HIV-associated infections also cause side effects, which may be similar to the clinical symptoms and signs of HIV infection. Most side effects can be easily managed.

Side effects can be graded into mild (grade 1), moderate (grade 2), severe (grade 3) and potentially life threatening (grade 4).

All antiretroviral drugs may have side effects.

4-36 Should patients be warned about side effects?

It is very important that patients know the common side effects of the antiretroviral drugs that they are taking. It is also important that patients know which side effects to look out for and which can be serious. If side effects are mild, patients should not stop the antiretroviral drugs. With severe side effects they should report immediately to the clinic. Educating patients about side effects is an important part of care. All patients on antiretroviral treatment must be able to monitor themselves for side effects.

Patients should be educated about side effects.

4-37 What are the common side effects of antiretroviral drugs?

Tiredness, nausea and vomiting, headaches and diarrhoea are common and may be caused by all classes of antiretroviral drugs. These side effects are not serious and usually settle after the first few days or weeks. It is important that patients continue with their antiretroviral drugs in spite of mild side effects. Sometimes other medication can be taken to help relieve these symptoms (paracetamol for headache and antiemetics for nausea and vomiting). Taking antiretroviral treatment with food often helps reduce side effects. Side effects, no matter how mild, must always be reported to the staff. Fortunately, most side effects are mild. Most patients will not experience side effects.

Most patients experience no side effects.

NOTE Severe vomiting or diarrhoea may cause dehydration as well as reduce absorption of medication.

4-38 When do most side effects occur?

Most side effects occur in the first six weeks of starting antiretroviral treatment. They usually get better on

their own after one to two months. However, some serious side effects may occur at any time that antiretroviral drugs are taken.

4-39 What serious side effects may occur with antiretroviral drugs?

1. Rash
2. Hepatitis
3. Anaemia
4. Peripheral neuropathy
5. Renal failure
6. Wasting and accumulation of fat (lipodystrophy)
7. Pancreatitis
8. Lactic (metabolic) acidosis
9. Severe vomiting or diarrhoea

4-40 What rashes occur commonly with antiretroviral drugs?

1. Mild rashes are common and include a localised or generalised erythematous (pink), maculopapular (measles-like) or urticarial rash with no other symptoms.
2. Severe rashes include any rash with blistering, peeling or involvement of the mucous membranes of the mouth and conjunctivae. A severe rash may also present together with fever, a fast pulse or abdominal pain (due to hepatitis). Severe rashes are due to a hypersensitivity reaction and can be fatal.

Rashes are common with antiretroviral treatment and usually are caused by 'non-nucs', especially nevirapine. TDF may also cause a rash. These rashes almost always occur in the first six weeks of treatment.

Nevirapine and efavirenz commonly cause skin rashes.

Remember that HIV infection itself and drugs used to treat HIV-associated infections (especially co-trimoxazole) also commonly causes rashes. Therefore the rash may not be due to the antiretroviral drugs.

NOTE Severe rashes due to a hypersensitivity reaction may result in Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). Constitutional symptoms such as fever are also present and warn of a dangerous side effect. Always look for hepatitis with severe drug rashes.

4-41 How should skin rashes be managed?

Nevirapine must always be started at half doses (i.e. 200 mg once daily) for the first 14 days as this reduces the risk of a rash. Continue treatment if the rash is mild. Do not increase the dose of nevirapine until any rash has settled.

All patients with a severe rash must be referred to an antiretroviral clinic urgently. If this cannot be done on the same day, stop all three antiretroviral drugs immediately and send the patient to an antiretroviral clinic as soon as possible. Usually nevirapine is swapped for a 'PI'. These patients must never be given a 'non-nuc' again (i.e. neither nevirapine nor efavirenz should ever be prescribed again).

NOTE Severe side effects with nevirapine are more common if antiretroviral treatment is started in patients who have

a high CD4 count, above 250 cells/µl in women and 400 cells/µl in men.

All antiretroviral drugs must be stopped immediately if a severe rash occurs.

NOTE Steroids and antihistamines do not help most sensitivity rashes caused by nevirapine.

4-42 Which antiretroviral drugs cause hepatitis?

All classes of antiretroviral drugs can cause hepatitis. However, nevirapine is the drug which is usually associated with hepatitis. Efavirenz can also cause hepatitis but less commonly.

Hepatitis due to nevirapine is most common in patients, especially women, who have a high CD4 count before the start of treatment.

Liver function tests (ALT, i.e. alanine amino transferase) should be done on all patients when nevirapine is started and also should be checked if a patient on efavirenz or nevirapine develops a rash or symptoms of hepatitis.

Hepatitis is usually caused by nevirapine.

NOTE Nevirapine causes asymptomatic hepatitis in 10% and clinical hepatitis in 1% of patients. Nevirapine plus TB treatment increases the risk of severe rash and hepatitis. d4T and co-trimoxazole may also cause hepatitis with raised enzymes. Nucleoside reverse transcriptase inhibitors may cause a fatty liver (steatosis).

4-43 What are the clinical signs of hepatitis?

Hepatitis may be clinical (nausea, loss of appetite, jaundice, enlarged liver, itching and abdominal pain) or asymptomatic (when it is diagnosed by finding raised liver enzymes in the blood without any clinical signs of hepatitis). An ALT level above three times normal (normal below 40 iu/l) indicates an increased risk of hepatitis.

NOTE Liver damage can be severe and permanent, but rarely fatal.

4-44 What is the management of a patient with hepatitis?

Patients with asymptomatic hepatitis and only mildly raised liver enzymes (up to five times normal) can be followed clinically without stopping the drugs. The hepatitis usually resolves. Using a low dose of nevirapine (200 mg daily) for the first two weeks lowers the risk of hepatitis (and rash).

Patients with clinical hepatitis or asymptomatic hepatitis with markedly raised liver enzymes should be urgently referred to an antiretroviral clinic where stopping all treatment may be considered.

4-45 Is anaemia a common problem with antiretroviral drugs?

Anaemia (Hb below 10 g/dl) is seen in few patients receiving AZT. These patients may appear pale and feel weak and dizzy. Anaemia is usually mild and the AZT need not be stopped.

A haemoglobin level and differential count or full blood count should be done when AZT is started and should be repeated at four weeks, eight weeks, 12 weeks and 24 weeks. Patients with a haemoglobin level below 8 g/dl due to AZT should have the AZT dose reduced or should swap the AZT for another NRTI.

Anaemia is a side effect of AZT.

NOTE With severe anaemia (haemoglobin less than 6.5 g/dl) it is important to stop AZT and replace with TDF. A blood transfusion may be needed. Patients with an Hb between 6.5 and 8 g/dl should be closely followed. The AZT dose can be reduced to 200mg twice daily.. AZT also causes neutropenia but does not lower the platelet count.

4-46 What is peripheral neuropathy?

This is a problem which affects the peripheral nerves, especially in the legs. It presents with pain, numbness and abnormal sensation in a 'glove and stocking' distribution. Most patients with peripheral neuropathy present with painful feet at night.

Peripheral neuropathy is usually caused by 'nucs' which have a 'd' in their names, e.g. ddI and d4T. These drugs should not be used together as this increases the risk of peripheral neuropathy. Depending on the severity of the neuropathy, the drugs may have to be changed, after consultation with an HIV clinic, as the peripheral neuropathy can become worse if the drug is continued. The symptoms of peripheral neuropathy usually slowly improve after the drugs have been stopped. Other drugs, such as INH and alcohol may also cause peripheral neuropathy.

d4T and ddI are associated with peripheral neuropathy and should not be used together.

NOTE d4T is the commonest cause of peripheral neuropathy. It may need to be swapped for TDF.

4-47 What is lipodystrophy?

This is an abnormal distribution of subcutaneous fat resulting in a change in body shape. Fat is lost (lipoatrophy) from the face and limbs and gained (accumulated) over the abdomen, back of the neck and breasts. Unfortunately lipodystrophy is not usually corrected when the antiretroviral drugs are changed. Many patients gain weight when antiretroviral treatment is started. Lipodystrophy is usually caused by ddI, d4T, efavirenz and the PIs.

Lipodystrophy is a redistribution in body fat and is usually associated with d4t and ddI and the PIs.

NOTE Lipodystrophy with central obesity and peripheral wasting may be associated with insulin resistance and fasting hyperlipidaemia with a raised plasma cholesterol and triglyceride concentration (the lipodystrophy syndrome). Marked hypertriglyceridaemia can cause pancreatitis while a raised serum

Table 4-2: *Summary of side effects of antiretroviral drugs.*

Name of drug	Major side effects
'Nucs'	
TDF	Renal failure, rash, fractures
3TC	Few side effects
AZT	Nausea and vomiting, anaemia, neutropenia
d4T	Peripheral neuropathy, pancreatitis, lactic acidosis, lipodystrophy
ddI	Peripheral neuropathy, pancreatitis, lactic acidosis, lipodystrophy
'Non-nucs'	
Nevirapine	Severe rash, hepatitis
Efavirenz	Emotional or psychiatric symptoms, rash
'PIs'	
Ritonavir	Lipodystrophy
Lopinavir/ritonavir	Diarrhoea, lipodystrophy

cholesterol increases the risk of coronary heart disease.

4-48 Which drugs may cause lactic acidosis?

Lactic acidosis is a rare but serious and potentially fatal side effect of 'nucs', particularly d4T and ddI. Therefore these drugs must never be used together. It usually only occurs more than six months into treatment when patients have responded well and are clinically improving with good adherence. It is most common in women who are overweight or pregnant. Patients with lactic acidosis present with a gradual onset of tiredness, weight loss and abdominal complaints (nausea, vomiting, abdominal pain or discomfort). Always suspect lactic acidosis if patients, who have been well and gaining weight for months, start to lose weight. Lactic acidosis has become a rare side effect of ART since the introduction of TDF in first line treatment instead of d4T.

Lactic acidosis is a rare but serious side effect of 'nucs' and occurs after months of good response to treatment.

Patients with suspected lactic acidosis must be immediately taken off all treatment and urgently referred to an HIV treatment centre for investigation and management.

NOTE Hyperlactataemia (serum lactate above 2 mmol/l) and lactic acidosis often with hepatic steatosis (fatty liver), liver failure, pancreatitis or peripheral neuropathy, are due to mitochondrial damage as 'nucs' also interfere with the replication of mitochondrial DNA. Asymptomatic hyperlactaemia (without acidosis) is common (up to 20%) while symptomatic hyperlactaemia (without acidosis) occurs in 1% and hyperlactataemia with lactic acidosis in 0.1% of patients on 'nucs'. The risk is lower with AZT than d4T. TDF, ABC and 3TC are relatively safe and can be started once the lactate has returned to normal.

4-49 Which drugs cause pancreatitis?

Pancreatitis (inflammation of the pancreas) is another severe complication of d4T and ddI, especially when they are used together. Alcohol abuse may increase the risk of pancreatitis.

Pancreatitis presents with vomiting, abdominal pain and tenderness. The drugs must be stopped immediately and the patient urgently referred.

Abdominal pain or discomfort is an important symptom in patients on antiretroviral treatment as it may be due to hepatitis, lactic acidosis or pancreatitis.

NOTE The serum amylase and lipase levels are raised in pancreatitis.

4-50 What is the management of severe vomiting or diarrhoea?

Some antiretroviral drugs cause nausea and vomiting or diarrhoea. The problem is usually mild and settles after a few weeks. However, vomiting may be severe (especially with AZT) while diarrhoea may also be severe (especially with Aluvia). This can lead to dehydration. Taking medicine with food and anti-nausea medication may help reduce vomiting. Efavirenz should be taken without food if it causes vomiting.

Oral rehydration solution will help prevent or correct dehydration. Patients with signs of severe dehydration should be urgently referred to hospital.

4-51 Should antiretroviral drugs rather not be used because of their side effects?

No. Antiretroviral drugs are a very important part in the treatment of HIV infection and the only way of managing AIDS. Like most other drugs, they have side effects. Usually side effects are mild and the antiretroviral drugs need not be stopped. Most patients have no or only mild side effects. However, both patients and health workers should know the symptoms and signs of severe side effects. If these appear the drugs must be stopped immediately and the patient referred urgently to an antiretroviral clinic for assessment.

The advantages of antiretroviral drugs far outweigh the side effects.

4-52 When do side effects occur?

1. They may occur early during the initiation of treatment (the first few weeks or months of treatment).
2. They may occur later when treatment is stabilised (after many months).

4-53 Which side effects occur during early treatment?

Minor side effects are common, e.g. nausea, vomiting, diarrhoea, headaches, muscle pains, sleeplessness, minor rashes. However, serious side effects such as serious rashes and hepatitis may also occur early and need to be looked out for.

Most minor side effects during the initiation of antiretroviral treatment get better over time without any treatment.

Peripheral neuropathy may also occur early in treatment.

4-54 Which side effects occur during later treatment?

1. Lipodystrophy and fat wasting
2. Lactic acidosis
3. Peripheral neuropathy

NOTE Some other metabolic disorders can occur later in treatment (with or without lipodystrophy) including high cholesterol and glucose levels.

4-55 Do patients lose weight on antiretroviral treatment?

Normally patients feel better and gain weight when antiretroviral treatment is started. Therefore weight loss on antiretroviral treatment is an important danger sign. It may be due to common early side effects such as nausea, vomiting or diarrhoea. However, weight loss in patients who have previously been well may also indicate the development of lactic acidosis.

Many patients on antiretroviral treatment complain of hunger once their immune system starts to recover. This may be a problem in poor people who cannot afford to buy more food.

4-56 Should one drug be stopped if side effects are severe?

It may be necessary to stop an antiretroviral drug if severe side effects occur, e.g. severe rash or clinical hepatitis. If this is done, all drugs must be stopped together. Stopping one drug will lead to resistance of the remaining two drugs. The drug combination must be carefully examined as the problem drug may have to be swapped or a different combination may be needed. Changing drugs must always be done at an antiretroviral clinic by an HIV expert. HIV infection must never be treated with only one or two drugs. A full combination of three drugs is always needed.

If necessary, stop all antiretroviral drugs and not just one drug.

4-57 Which antiretroviral drug should not be used during pregnancy?

Most antiretrovirals are safe in pregnancy. Previous anxiety about Efavirenz causing congenital malformations (birth defects) appears to be unfounded.

4-58 Do any antiretroviral drugs cause renal damage?

TDF can cause renal damage, which presents as a drop in creatinine clearance. Therefore creatinine clearance should be monitored at

one month, three or four months, six months and then 12-monthly thereafter, when the drug is used. Do not use TDF if the creatinine clearance is less than 60 ml/min.

NOTE TDF may also cause a rash and, on rare occasions, decrease phosphate levels, resulting in bone fractures.

TDF can cause kidney damage.

Case study 1

A patient with HIV infection, who has been treated with AZT alone for two weeks by a general practitioner, is referred to an HIV clinic. The patient complains of headache, nausea and feeling generally unwell since the treatment was started.

1. Do you agree with AZT alone as acceptable treatment for AIDS?

One or two drugs alone should *never* be used to treat HIV. Three drugs are always used together (multi-drug therapy), e.g. AZT, 3TC and lopinavir/ritonavir.

2. What is the advantage of using multiple drugs?

There is a higher rate of successful treatment with less drug resistance.

3. Why is this patient complaining of headache, nausea and feeling unwell?

These are common side effects of AZT. Mild side effects of antiretroviral treatment usually settle on their own after a few weeks. Unless the side effects are serious, treatment should not be stopped. Mild side effects can be treated symptomatically.

4. What is an important side effect of AZT?

Anaemia. Therefore the haemoglobin concentration should be monitored in patients receiving antiretroviral treatment which includes AZT.

5. What class of drug is AZT?

TDF, AZT, 3TC, d4T, ABC and ddI are 'nucs'. They all block an important enzyme and thereby prevent HIV from infecting CD4 lymphocytes. 'Nucs' are used in most multi-drug regimens to treat HIV.

6. What are the main goals of antiretroviral treatment?

To suppress the multiplication of HIV. This will allow the immune system to recover (increased CD4 count), improve the patient's clinical condition and decrease the risk of death.

Case study 2

A young woman who has HIV infection presents at an HIV clinic with the hope of being cured. She wants to start a family as soon as she is well again.

1. Can antiretroviral treatment cure HIV infection?

Unfortunately not. However, it can markedly improve the patient's health and make HIV infection a chronic but manageable disease.

2. What treatment should she receive?

She should be given a standardised regimen. Once she has been prepared for treatment, a first-line combination of TDF, FTC and efavirenz will be started.

3. What is a standardised regimen?

This is a fixed combination of antiretroviral drugs. There are many advantages to a standardised regimen over an individualised regimen. With an individualised regimen each patient is given their own combination of antiretroviral drugs.

4. What are the advantages of a standardised regimen?

It is simpler, safer and cheaper to use with fewer side effects and drug interactions. The education and training of both patients and staff is much easier. Tuberculosis is also treated with a standardised fixed combination of drugs.

5. What first-line regimens are used in South Africa?

The first line regimen of choice is TDF plus FTC and efavirenz as a once daily combination tablet.

Other first line regimens are:

1. AZT, 3TC and efavirenz if there is a contraindication to TDF
2. TDF, 3TC and nevirapine if there is a contraindication to efavirenz

6. Which 'non-nuc' would you choose for this woman?

Efavirenz is the 'non-nuc' of choice, particularly if her CD4 count is above 250cells/μl as people with high CD4 cell counts have an increased risk of hepatitis when starting nevirapine.

Case study 3

A patient has recently started on a first-line regimen with nevirapine. Three weeks after starting antiretroviral treatment he develops a fever and feels ill with a generalised blistering skin rash which also involves his mouth.

1. Are skin rashes common with nevirapine?

Yes. They are usually mild and the patient does not feel generally unwell. With continued antiretroviral treatment most mild skin rashes caused by nevirapine will disappear.

2. Would you be concerned about this patient's skin rash?

Yes, because this is a serious rash and the patient is ill with a fever. Any blistering skin rash, especially if it involves the mouth, is potentially life threatening. All drugs must be stopped immediately and the patient should be referred urgently to hospital. Nevirapine will have to be replaced (swapped) with a 'PI' such as Aluvia.

3. Should this patient be given efavirenz instead of nevirapine?

No. This patient must never again be given a 'non-nuc' (either nevirapine or

efavirenz) as the severe reaction is likely to recur.

4. What other serious side effect may be caused by nevirapine?

Hepatitis. Clinical hepatitis presents with nausea and vomiting, abdominal pain and jaundice. A rash and hepatitis may occur together. Patients with any signs of hepatitis must be urgently referred to hospital. Severe hepatitis can be fatal.

5. How can the risk of side effects with nevirapine be reduced?

By starting with a smaller dose for the first two weeks of treatment (one tablet at night only).

6. Should patients be warned about side effects?

It is very important that patients be well educated about the symptoms and signs of the common side effects before antiretroviral treatment starts. They should immediately report any side effects.

Case study 4

During preparation for antiretroviral treatment a group of patients is fully informed about the drugs they are going to take. One patient is afraid of starting treatment when he learns about the possible side effects. A friend of his developed very painful legs after antiretroviral treatment was started.

1. What information about the antiretroviral drugs should patients be given?

They must know the names and appearances of the drugs in the first-line combination. They must know how many drugs to take and when they should be taken.

2. How many times a day are antiretroviral drugs taken?

Some drugs in the first-line combination (AZT and 3TC) are taken twice a day (12-hourly) while TDF and Efavirenz are taken once a day. Some formulations of 3TC also allow once daily dosing. Nevirapine is taken once a day to start, but later is also taken twice a day.

3. Should antiretroviral drugs be taken with meals?

Most antiretroviral drugs in the first-line combination should be taken with meals as this reduces the risk of side effects. For the first few weeks efavirenz should be taken on an empty stomach. Second-line drugs are also taken with meals.

4. Should patients who are afraid of the side effects rather not take antiretroviral drugs.

No. Antiretroviral drugs are the only way to effectively treat patients with HIV. Without antiretroviral treatment they will die. Most patients have no or only mild side effects.

5. Which antiretroviral drugs cause painful legs?

Pain and numbness of the hands and feet are due to peripheral neuropathy. This is usually caused by d4T or ddI. Therefore, these two drugs should never be used together as this increases the risk of peripheral neuropathy. Other drugs such as INH and alcohol may also cause peripheral neuropathy.

Case study 5

After failing treatment with the first-line combination of antiretroviral treatment a patient is started on the second-line combination. She feels much better on the new treatment. However, after a few months she notices that her face is becoming wasted and she is gaining weight around her abdomen.

1. What antiretroviral drugs are used in the second-line combination?

This depends on the first line regimen but the usual combination is AZT and 3TC plus lopinavir/ritonavir.

2. What class of drugs are these?

AZT and 3TC are 'nucs'. As with the first-line combination, 'nucs' are an important part of the multi-drug regimen. Aluvia is a combination of two 'PIs' (ritonavir and lopinavir). The second-line combination therefore includes 'PIs' but not 'non-nucs'.

3. How should lopinavir/ritonavir be taken?

Twice a day with meals.

4. What are common minor side effects with lopinavir/ritonavir?

Nausea and loose stools. These are less troublesome if the medication is taken with meals.

5. Why is this patient developing wasting of the face?

Unfortunately peripheral wasting of the face and limbs and central fat accumulation over the stomach and back of the neck may occur with AZT and the 'PIs'. This change of body shape due to the redistribution of fat does not always resolve if these drugs are stopped.

6. What is the name of this condition?

Lipodystrophy.

5

Management of patients on antiretroviral treatment

Before you begin this unit, please take the corresponding test to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- Describe the first treatment visit.
- List the schedule of follow-up visits.
- Explain what is done at each visit.
- List what blood tests are needed.
- Define treatment success and failure.
- Manage patients on successful treatment.
- Manage patients with failed treatment.
- Promote excellent adherence.
- Explain the dangers of drug resistance.
- Describe the immune reconstitution syndrome.

Starting antiretroviral treatment

5-1 What are the goals of antiretroviral treatment?

1. The patient should feel well and have few illnesses related to HIV infection.
2. The CD4 count should increase and remain above the baseline count.
3. The viral load should become undetectable and remain undetectable.

Antiretroviral treatment reduces the multiplication of HIV and this allows the immune system to recover. As a result the patient loses the symptoms and signs of HIV infection and is able to return to a normal lifestyle. Antiretroviral treatment therefore decreases both the morbidity and mortality related to HIV. Antiretroviral treatment is best started at an antiretroviral clinic. Antiretroviral therapy may also be started in a TB clinic for TB patients, at a MOU for pregnant women or in a hospital or hospice for very sick patients.

The main goal of antiretroviral treatment is to get the patient well again.

NOTE An extended programme of free antiretroviral treatment was started in South Africa in 2004.

5-2 What is an antiretroviral clinic?

This is a clinic where antiretroviral treatment is started and managed. Patients are referred to the antiretroviral clinic when they have met the criteria for treatment. An antiretroviral clinic is staffed by doctors and nurses who have had special training in the use of antiretroviral drugs and the management of patients on these drugs.

5-3 What is the first antiretroviral treatment visit?

This is the visit when antiretroviral treatment is started (i.e. commencement visit). Patients should already have been prepared for antiretroviral treatment at one or two screening visits. A decision would already have been made that the patient is 'treatment ready' and baseline blood tests done. A final check is made that the patient is fully prepared for treatment. At the first antiretroviral treatment visit the following should be done:

1. A second count of co-trimoxazole tablets is done to assess adherence.
2. The importance of excellent adherence is again stressed by the counsellor.
3. The patient sees the doctor or nurse for the final instructions and support. A detailed description of the drugs and their doses is given using a treatment chart. A graphic treatment chart is very useful and should be given to each patient.
4. The patient should be given a patient-carried treatment card.
5. The patient's details are entered into the antiretroviral treatment register or electronic database.
6. An HIV summary record is started which will be kept by the clinic and updated by the doctor or nurse at each visit. Examination notes from the screening visits should be included.
7. The instructions and dosing are reinforced by the nurse. The instructions must be clearly written on the pill container with a permanent marker.
8. The patient is given one month's supply of drugs by the pharmacist.
9. Each person in the team makes sure that the patient understands which medicine to take, how much and when. They also check that the patient knows the side effects of the drugs to be taken and the importance of excellent adherence.

5-4 What is a patient-carried HIV treatment card?

This is a treatment card kept by the patient (similar to the antenatal cards and Road-to-Health cards). It includes all the important information about the patient's management. Patient-carried cards are a very important tool in helping patients become responsible for their care. It also improves

communication between health facilities. Managing HIV infection like any other disease helps to reduce stigma.

5-5 What antiretroviral regimen is used for first-line treatment?

Almost all patients are started on the first-line single dose combination tablet of TDF, FTC and efavirenz. Nevirapine may be used instead of efavirenz for patients with psychiatric disorders or other contraindications to efavirenz. Some patients who have already been started on d4T, and who haven't experienced side effects, may remain on d4T.

Treatment is almost always started with the first-line combination of antiretroviral drugs.

5-6 What other medication will be given?

Co-trimoxazole prophylaxis will be continued until the CD4 count is above 200 cells/µl. This usually implies that prophylaxis is continued for at least the first six months of antiretroviral treatment.

5-7 How often are these patients seen at the antiretroviral clinic?

Usually patients are seen at the antiretroviral clinic at one, two and three or four months after starting treatment.

Patients who are taking nevirapine have an extra visit two weeks after starting treatment as they need to be assessed for possible side effects and the dose of nevirapine needs to be increased from the starting dose of one tablet daily to one tablet twice daily at this visit.

5-8 How often should education and counselling be offered?

At every clinic visit. The importance of excellent adherence and support must always be stressed. Patients must have an opportunity to ask questions or discuss problems.

The patient should be counselled at every visit.

5-9 Who are the members of the multidisciplinary team at the antiretroviral clinic?

1. The doctor or ART trained nurse, who should take a history and perform a general examination at the first treatment visit, and again if necessary at follow-up visits.
2. The nurse, who should see the patient to complete the treatment register and take the necessary blood samples. The nurse should also check adherence at every visit.
3. The counsellor/educator, who should see the patient at every visit.
4. The pharmacist, who should provide the antiretroviral drugs and advise the patient on how to take them every time medicines are dispensed.

Trained lay counsellors and community care workers are very important members of the health team.

Follow-up visits

5-10 What should be done at the follow-up visits?

1. A history is taken for adherence, side effects and any other problems.
2. A general examination is completed.
3. The patient is weighed.
4. A pill count is done before the patient sees the doctor or nurse.
5. The patient is counselled.
6. Routine blood samples are taken if indicated.
7. Family planning is discussed with women.
8. Condoms are dispensed.

5-11 How often are the medicines given by the clinic?

Monthly to 3-monthly. A missed visit for medication suggests poor adherence. When medicine is collected, the patient should also be seen by a nurse or counsellor who will assess adherence and ask about side effects. Excellent adherence must be promoted at every visit. The antiretroviral treatment register or electronic database must be updated each time medication is provided.

5-12 What blood tests are routinely done during the first year of first-line treatment?

1. Creatinine clearance monitoring is done at three, six and twelve months for patients on TDF.

   NOTE Some guidelines recommend monitoring of creatinine clearance earlier in treatment e.g. the 2013 Western Cape Antiretroviral guidelines recommends monitoring at one, four and twelve months.

2. A haemoglobin level and differential count should be done at one, two, three and six months for patients taking AZT.
3. The liver function is not routinely monitored on treatment but an ALT should be checked at any time if the patient develops a rash or has signs or symptoms of hepatitis.

   NOTE The normal range for serum ALT is 5 to 40 u/l. Any patient with an ALT above five times the upper limit of normal (200 u/l) requires an immediate review. There is an increased risk of drug induced hepatitis in patients with hepatitis B or C co-infection.

5-13 What monitoring for side effects is needed for other antiretroviral drugs?

Clinical monitoring without blood tests is adequate for 3TC, efavirenz and d4T provided the patient is clinically well.

5-14 How should patients be followed up after three months?

Most of the side effects will have cleared by three months. Patients should also be into the routine of taking their antiretroviral drugs regularly. Few problems are expected after three months therefore patients, will then only be seen by a doctor six-monthly. They may collect their medicines every one to three months.

Some antiretroviral clinics are able to follow their patients for six months after starting treatment. However, some patients can be referred back to the

HIV clinic sooner or may be enrolled in adherence clubs for long term support during treatment.

Monitoring the response to anti-retroviral treatment

5-15 How is the response to antiretroviral treatment assessed?

1. By the clinical response
2. By the viral load
3. By the CD4 count

5-16 What is the expected clinical response to antiretroviral treatment?

With successful treatment patients should start to feel and look well again. Most patients develop a good appetite and gain weight. Associated infections such as thrush and diarrhoea disappear and skin rashes clear up. The clinical response follows the gradual recovery of the immune system. By three months patients should notice a big difference in their general health.

5-17 What is the viral load?

The viral load is a measure of the amount of HIV in the blood. The higher the viral load, the faster HIV is multiplying. Therefore, a high viral load indicates that there is a lot of HIV in the blood (and other body secretions). Viral load is usually expressed as RNA copies/ml (which is the same as copies/ml).

The viral load is a measure of the amount of HIV in the blood.

NOTE The viral load is the concentration of free virus in the plasma. In its free form HIV is an RNA virus. Therefore the RNA PCR test is used to measure the viral load.

5-18 What is the range of viral load results?

People with HIV infection can have a viral load ranging from less than 50 copies/ml to several million copies/ml. A viral load of less than 50 copies/ml is regarded as 'undetectable'.

5-19 What is the value of knowing the viral load?

The viral load is the best indicator of the response of the immune system to antiretroviral treatment. With successful treatment the viral load will steadily drop until it is undetectable (less than 50 copies/ml). Measuring the viral load is of very little value before antiretroviral treatment is started.

Viral load is the best indicator of the success of antiretroviral treatment.

NOTE The viral load is the best measure of the rate at which the infection will progress. The higher the viral load, the sooner the person will become ill. Patients with symptomatic HIV infection have a higher viral load than people with HIV infection who are still well. A patient with a viral load above 6 log has a poor prognosis without urgent antiretroviral treatment.

5-20 How is the viral load expressed?

The viral load is expressed as copies/ml or a log value. The log value is preferred if the change in viral load is determined. If the viral load drops by 1 log the number of copies/ml will fall by a factor of 10. Similarly a 2 or 3 log drop means that the number of viral copies has decreased 100 or 1000 fold respectively. The log value will fall by 0.3 if the number of viral copies is halved.

Log values are used to measure changes in viral load.

NOTE Only a change in viral load of greater than 0.5 log is significant.

5-21 What viral load indicates a good response to treatment?

If the response to antiretroviral treatment is good the viral load should fall by 1 log within six weeks. (See 5-25.)

5-22 What are viral 'blips'?

These are transient (short-lived) increases in the viral load of patients who are being successfully treated. They may be caused by an acute infection or an immunisation. Therefore, it is important that the viral load is not measured when the patient is ill.

5-23 When should the CD4 count and viral loads be measured?

Viral loads should be measured once at 4 to 6 months and again 12 months after starting treatment and every 12 months thereafter. The CD4 count should be measured at 12 months after starting treatment and if <200cells/µl should be repeated at 6 monthly intervals until two consecutive CD4s are >200cells/µl .

NOTE Should funding permit, more frequent CD4 and viral load monitoring is preferable and should be done every 4 to 6 months for tighter control of treatment.

5-24 What change should take place in the CD4 count by six months?

The CD4 count should increase. People with CD4 counts below 200 cells/µl may expect an increase of 80% or more.

NOTE The CD4 count should be increasing by four months after starting treatment. The lower the CD4 count at the start of antiretroviral treatment, the slower will be the return to normal.

5-25 What change should take place in the viral load by four to six months?

The viral load should be undetectable (less than 50 copies/ml).

5-26 What is the best indicator of treatment success?

An undetectable viral load.

An undetectable viral load is the best indicator of successful treatment.

5-27 What should be done if the treatment is successful?

If the treatment is successful with an undetectable viral load by six months, the patient should be followed at the ART clinic and seen every three

months. The CD4 count and viral load should be measured 12-monthly to determine whether the treatment has remained successful or not. Adherence should be supported at every clinic visit.

5-28 For how long can treatment remain successful?

For many years. Provided drug adherence is excellent, viral resistance is unlikely to develop and a long-lasting response to multi-drug treatment can be expected (15 to 20 years with excellent adherence).

Antiretroviral treatment can be successful for many years.

5-29 What is treatment failure?

The features of treatment failure after six months on antiretroviral therapy are:

1. A viral load above 1000 copies/ml
2. A CD4 count that has not increased above the baseline level

Progression of the clinical disease with further development of HIV-associated infections or malignancies despite antiretroviral treatment should always suggest treatment failure.

NOTE Some patients with a very low CD4 count at the start of treatment may fail to show a rise in the CD4 count despite good viral suppression and clinical improvement.

5-30 What should be done if the first-line treatment is unsuccessful?

These patients and their management must be carefully reviewed before a change in treatment is made. Treatment failure may be due to poor adherence or may occasionally occur in spite of excellent adherence.

1. If adherence is poor, every effort must be made to improve adherence. The causes of poor adherence must be found and corrected if possible. If the viral load is 50 to 1000 copies/ml, the viral load should be repeated in six months after active intervention to improve adherence; but if the viral load is above 1000 copies/ml it should be repeated sooner (in three months), again after an active intervention to improve adherence. If the viral load remains high, even with poor adherence, the patient should start preparation for second-line treatment.
2. If adherence appears to have been good, drug resistance may still have occurred through one or two missed or delayed doses and a change in drug regimen to the second-line combination should also be made. Good adherence with a viral load above 1000 copies/ml is usually an indication for a change in drug regimen. Always repeat the viral load after an adherence intervention before considering a regimen change.

Always repeat the viral load measurement before considering a change in regimen.

5-31 Can previous exposure to antiretrovirals lead to treatment failure?

Yes. If first-line treatment including nevirapine in a woman has failed, despite excellent adherence, make sure that she was not given nevirapine for the prevention of mother-to-child transmission of HIV. Previous exposure to nevirapine is not a contraindication to standardised first-line treatment. However, treatment of patients who have been exposed to any antiretroviral drugs before must be discussed with an antiretroviral expert before starting treatment.

NOTE Patients who have previously been exposed to one or more antiretroviral drug(s) are no longer 'antiretroviral naive' and may already be resistant to one or more of these drugs.

5-32 What should be done if first-line treatment has failed despite excellent adherence?

Change from first-line to second-line treatment. The choice of the second-line combination depends on the drugs used in first line treatment.

If first line treatment consisted of TDF, 3TC or FTC plus efavirenz, change to a second line regimen of AZT, 3TC and lopinavir/ritonavir.

NOTE Check hepatitis B status before changing from a first line containing TDF as TDF and 3TC/FTC are also used to treat hepatitis B. If patient is Hep B surface antigen positive maintain patients on TDF and 3TC/FTC i.e. the second line regimen will be TDF + AZT + 3TC or FTC + Aluvia.

If first line treatment consisted of d4t or AZT plus 3TC and efavirenz, change to a second line regimen of TDF, 3TC and lopinavir/ritonavir.

NOTE 3TC is recycled in the second line regimen. Although the virus will almost certainly be resistant to 3TC this resistance results in a greater susceptibility to TDF, AZT and d4t and the mutated virus does not replicate as well.

5-33 How is the second-line of treatment managed?

The schedule of visits is the same as that for the first-line combination with a commencement visit followed by visits at one, two and three or four months. Patients are then seen again at six months followed by three-monthly visits.

5-34 What routine blood tests are done with second-line treatment?

Patients receiving AZT should have a baseline Hb and diff before the start of treatment followed by a Hb and diff at one, two, three and six months, as AZT may suppress the bone marrow.

Patients on lopinavir/ritonavir should have a baseline fasting blood glucose, cholesterol and triglyceride measurement. This should be repeated at three months.

NOTE Some guidelines recommend a fasting cholesterol and triglycerides for patients on lopinavir/ritonavir at baseline, 4 months, 12 months and then every 12 months.

5-35 What should be done if the second-line treatment fails?

If failure is due to poor adherence, every effort must be made to improve adherence. If adherence is excellent and the patient becomes clinically worse on the second-line combination, the patient should still continue with the treatment. Antiretroviral therapy has been shown to be lifesaving even in patients with a viral load up to 20 000 copies/ml.

NOTE Additional antiretroviral drugs can be used in new combinations in an attempt to control viral replication in patients who have failed on both first- and second-line treatment. This is a complex problem that must only be addressed by an ART specialist. Evidence shows that there may still be benefit in keeping patients on a failing regimen.

Problems with anti-retroviral treatment

5-36 What are the main problems with antiretroviral treatment?

1. Poor adherence
2. Viral resistance to drugs
3. Treatment failure
4. Drug interactions
5. Drug interruptions
6. Side effects
7. Immune reconstitution syndrome
8. Complete dependence on long-term medication
9. Expense

Adherence

5-37 What is adherence?

Adherence is the degree to which patients take their antiretroviral drugs correctly.

5-38 What is excellent adherence?

Excellent adherence is taking all the pills correctly every day. With excellent adherence, 95% of all doses must be taken (i.e. 19 out of 20 doses). This means that not more than three doses can be missed in a month. It is also important that the doses are taken at the same time each day. Taking all the drugs at the correct dose and at the correct time each day is very important if antiretroviral treatment is going to be successful. Antiretroviral treatment can suppress the viral load reliably only if adherence is excellent.

Not more than three doses a month should be missed.

NOTE Owing to the short half-life of antiretroviral drugs, blood levels fall rapidly if a single dose is missed. The correct dose must be taken at the correct time in the correct way.

Excellent adherence is the key to treatment success.

5-39 What is poor adherence?

Poor adherence is missing doses or taking doses at the wrong time. Any adherence of less than 95% is not good

enough (i.e. poor). Even adherence of 80 to 95% may be inadequate.

5-40 What are the dangers of poor adherence?

1. Drug resistance
2. Treatment failure
3. Increased morbidity and mortality

Every effort must be made to ensure excellent adherence. Without excellent adherence the progression of HIV will not be stopped.

Poor adherence increases the risk of treatment failure and drug resistance.

5-41 How is adherence measured?

The history given by the patient is an unreliable method of assessing adherence. Better methods include:

1. Counting tablets that have not been taken (pill count). Patients should be asked to bring all their tablets back to the clinic at every visit.
2. Daily record cards or dosing diaries.
3. Unannounced home visits with pill counts.

A simple card for recording each dose on a daily basis helps promote and assess excellent adherence.

5-42 What factors are associated with poor adherence?

1. Poor patient preparation for antiretroviral treatment
2. Inadequate home support
3. Poor relationship with the clinic staff
4. Alcohol or drug abuse
5. Depression or other emotional problems
6. Side effects to antiretroviral treatment
7. Adherence tends to become worse over time
8. Non-disclosure of HIV status

Note that excellent adherence does not correlate with gender, education level, socio-economic class or cultural background. Adherence can be excellent even in poor, under-developed communities.

5-43 How can adherence be improved?

Excellent adherence must be promoted before treatment is started and then promoted continually at every clinic visit. Patients must be encouraged to take an active and responsible role in their treatment.

1. Before starting antiretroviral treatment, patients must make a firm decision to take medication at the correct time every day for the rest of their lives. They must have a positive attitude and be ready to take antiretroviral treatment. A clearly understood treatment plan must be negotiated with the patient.
2. Patients must understand why adherence is important and know about the dangers of poor adherence. Education and counselling about adherence should be provided at every visit in the patient's home language. A supportive and non-judgemental approach is needed.
3. Give and monitor the adherence to treatment with co-trimoxazole for a

month before starting antiretroviral treatment.
4. The clinic staff should check on adherence at every visit. A pill count should be done. If adherence is poor, ask the patient why doses have been missed and re-educate about the importance of adhering to treatment.
5. Suggest practical reminders such as an alarm clock, or link the time of taking medication to a particular radio or TV programme or cleaning teeth. A cell phone message or pager call can be arranged. Get the patient to use a pill box where tablets for the day can be counted out beforehand. Counsellors who know the community well can often offer the best adherence advice that will be suitable to the patient's lifestyle.
6. Patients need constant monitoring, education, encouragement and support. Good preparation and long-term support is essential for excellent adherence.
7. If possible, they should disclose their HIV status to a friend or family member who can support them.
8. Regular support groups of other patients on antiretroviral treatment are very helpful.
9. Continuing education should be provided at every visit.
10. Side effects must be promptly and correctly managed.
11. Provide a more caring service.

Patients must be ready and prepared before starting antiretroviral treatment.

5-44 How can health workers provide a more caring service?

Adherence can be improved if the clinic provides a more caring service.

1. Healthcare providers must make every effort to establish a trusting relationship with each patient. If possible the patient should see the same dedicated carer at each visit.
2. The clinic should provide a safe environment where the patient can feel protected. Patients should feel they are welcome to come to the clinic with a problem on any day, not just on their appointment day.
3. Remember that acceptance and emotional support by the clinic staff are very important parts of good care. Regular update education and an evaluation of the quality of advice being given by health workers is important.
4. A patient should never be without the required medication. It is unacceptable for the clinic to run out of drugs.

A good, caring service by the clinic improves adherence.

5-45 What are the commonest reasons for missing a dose?

1. Forgot
2. Too busy or away from home
3. Too ill
4. Side effects
5. Angry or depressed
6. Other urgent family matters such as a sick child or death of a relative

It is very important to find out why doses have been missed and how adherence can be improved.

It is important to find out why doses are missed.

5-46 Can a dose be taken late?

If a dose is not taken at the correct time, it can still be safely taken when remembered. It is better to take the dose late than not at all.

5-47 Does it matter if the medication is vomited?

Yes. If the patient vomits up the pills or tablets, the dose should be taken again immediately. Vomiting more than one hour after the medication is probably not important.

5-48 What factor may cause poor absorption of drugs?

Taking ddI with meals results in poor absorption. Therefore ddI is always taken well before or well after a meal.

5-49 Is an HIV adherence programme the same as the 'DOT' programme?

No, there are differences. With the DOT programme (Direct Observation of Therapy) the responsibility for taking the anti-TB medication is shared between the patient and a supporter in the community. This has only had limited success due to the difficulty in finding reliable and motivated supporters. In the HIV programme, patients are motivated and helped to take responsibility for their own treatment. Although family and community support is still important, the main responsibility for taking the medication correctly every day is placed on the patients themselves.

However, in patients who are unable to maintain excellent adherence in spite of help and support, a DOT system, where the responsibility for taking antiretroviral drugs is given to another reliable person (a 'treatment partner'), may be useful.

5-50 What is a national HIV adherence programme?

It is hoped that the media and the general community will help in reminding people on antiretroviral treatment to take their medication. Reminders could be given over the radio or on television. As HIV is a national problem, it is important that the whole nation helps to make sure that there is excellent adherence to antiretroviral treatment in order to reduce the risk of HIV drug resistance and the further spread of HIV.

A national adherence programme is urgently needed.

Drug resistance

5-51 What is drug resistance?

Drug resistance in HIV occurs when the multiplication of HIV is not blocked completely by a particular drug combination. Drug resistance will lead to treatment failure.

5-52 Is drug resistance important?

Yes. The development of resistance to one or more antiretroviral drugs will reduce the chance of successful treatment to the individual. It will also increase the risk of other people in the community acquiring HIV infection which is resistant to those drugs. This can be disastrous to both the patient and the community.

Drug resistance can be disastrous to both the patient and the community.

NOTE Resistance is most common with 'non-nucs' and 3TC as resistance occurs after a single mutation. Resistance to lopinavir/ritonavir is uncommon.

5-53 How can drug resistance be avoided?

1. By using a combination of three drugs from two drug classes. This is the basis of standardised regimens.
2. By excellent adherence. The more frequently doses are missed, the greater is the risk of resistance to those drugs.

Excellent adherence to antiretroviral treatment is the best way of avoiding drug resistance.

5-54 Can resistance be caused by previous drug exposure?

Yes. Patients who have previously been given antiretroviral drugs ('non-naive patients') must be carefully assessed by an antiretroviral expert before one of the standard drug combinations is started. There is concern that nevirapine used in the prevention of mother-to-child transmission (PMTCT) may cause later drug resistance to nevirapine in mother or infant.

5-55 What is cross-resistance?

If HIV becomes resistant to one drug in a class it is often also resistant to some or all the drugs in the same class. This is called cross-resistance (i.e. HIV is resistant to drugs across a drug class). This is particularly common for 'non-nucs'. If patients are resistant to nevirapine there is a high chance that they will also be resistant to efavirenz. Drug resistance between classes is uncommon.

NOTE Drug resistance may be primary (when the person is infected by a virus which is already resistant to one or more drugs) or secondary (when the virus becomes resistant during the course of treatment). Primary resistance is relatively uncommon in South Africa with levels of <5% reported in Gauteng. However moderate levels (5-15%) of primary resistance to "non-nucs" have been reported in surveillance studies done in KZN in 2009.

Treatment failure

5-56 What are the two types of treatment failure?

Treatment failure is diagnosed when antiretroviral treatment fails to produce and maintain an adequate suppression of the viral load. There are two forms of treatment failure.

1. Treatment failure right from the start of treatment when the viral load does not fall as expected within six months.
2. There may initially be a good fall in viral load but the viral load later increases again despite continuing treatment.

5-57 How is treatment failure confirmed?

Before diagnosing treatment failure it is important to repeat the viral load measurement after three months. The diagnosis of treatment failure is confirmed if the viral load remains high or increases further. Sometimes the viral load will be increased at the time of the first measurement but falls with the second measurement. Transient rises in the viral load are called 'blips'. They are not uncommon, especially if there has been a viral or bacterial infection, or the patient has recently been immunised. Therefore, always repeat the viral load after three months before diagnosing treatment failure.

5-58 What are the causes of treatment failure?

There are a number of causes:

1. Poor adherence
2. Poor absorption
3. Adverse drug interactions
4. Infection with drug-resistant HIV

5-59 What is the commonest cause of treatment failure?

Poor adherence is by far the commonest cause of treatment failure.

Poor adherence is the commonest cause of treatment failure.

5-60 How should treatment failure be managed?

The cause of the high viral load must be determined as far as possible, and actively managed, *before* the viral load measurement is repeated. It is important that the treatment regime should not be changed until a careful assessment is done and all the options considered. The second measurement of the viral load is usually done three months after the first measurement.

The treatment regimen should not be changed in haste.

Drug interactions

5-61 What is a drug interaction?

This is the interference of one drug with another drug. Common examples of drug interaction are:

1. Two similar drugs compete with each other at their site of action.
2. One drug alters the rate at which another drug is broken down in the body. This may result in the blood level of the drug being too high or too low.
3. If two drugs have similar side effects, these side effects are more likely to occur and be more severe if the two drugs are used together.

5-62 Which antiretroviral agents should not be used together?

Using either the first- or second-line combinations for antiretroviral treatment avoids drug combinations which compete with each other.

NOTE AZT should not be used together with d4T due to their competing sites of action. ddI and d4T should be avoided in combination due to additive toxicities.

5-63 What is the effect of rifampicin on antiretroviral drugs?

Rifampicin, used in the treatment of TB, increases the rate at which some antiretroviral drugs are broken down by the liver. As a result, these drugs may not act adequately because their blood levels are too low.

1. Rifampicin causes no problems with 'nucs'.
2. Rifampicin causes some problems with 'non-nucs' and lowers blood level of these drugs, especially nevirapine. Efavirenz is less affected than nevirapine, therefore nevirapine is often changed to efavirenz when first-line antiretroviral treatment is being given at the same time as anti-TB treatment.
3. Rifampicin causes serious problems with 'PIs' as it lowers blood levels of most of these drugs by about 80%. Therefore higher doses of 'PIs' are needed when they are used with rifampicin. The dose of lopinavir/ritonavir (Aluvia) should be doubled from 2 tablets 12 hourly to 4 tablets 12 hourly when used with rifampicin. This should be done slowly over two weeks with monitoring of the patients liver function as high doses of lopinavir/ritonavir may cause hepatitis.

Higher than normal doses of 'PIs' are needed if used together with rifampicin.

NOTE Protease inhibitors alter the metabolism of many drugs by inhibiting the p450 enzyme system (especially CYP3A4) which is used to break down these drugs. Atazanavir cannot be used with rifampicin.

5-64 What is the risk of using INH together with antiretroviral therapy?

Peripheral neuropathy is a side effect of INH (isoniazid) as well as d4T and ddI. Therefore, the risk of peripheral neuropathy is greater if either d4T or ddI are used together with INH.

5-65 Can antiepileptic medication be used with ART?

Due to drug interactions with both PIs and NNRTIs, many commonly used antiepileptic medications cannot be used with ART. Patients on phenytoin, phenobarbital and carbamazepine should have their medication changed to sodium valproate (epilim) or lamotrogine before starting ART. The changeover of treatment should occur gradually to avoid precipitating siezures.

Sodium valproate or lamotrogine are the antiepileptic medications of choice for patients starting ART.

Drug interruptions

5-66 What is a drug interruption?

This is when antiretroviral treatment is stopped for a short period (a temporary interruption).

5-67 What are the reasons for drug interruptions?

Causes of drug interruptions are:

1. Intolerable side effects. Once the symptoms are under control treatment may be changed to another drug combination, or the same drug combination may be restarted.
2. Interaction with other drugs, e.g. TB treatment.
3. Patient unable to swallow due to severe oesophageal thrush.
4. Lack of drugs at the clinic. This should never happen but unfortunately it does.

5-68 What is the danger of drug interruption?

If only one antiretroviral drug is stopped there is a danger that resistance will develop to the remaining drugs. Therefore, it is best to stop all the antiretroviral drugs if drug interruption cannot be avoided. When stopping a regimen containing a 'non-nuc' the 'nucs' should be continued for one week after stopping the 'non-nuc'. This is because the 'non-nuc' remains for a longer period in the body than the 'nucs' and the continuation of the 'nucs' therefore ensures that the patient continues to receive triple therapy until the 'non-nuc' has been eliminated. This is referred to as "covering the tail of the 'non-nuc'". This decreases the chance of the patient developing resistance to the 'non-nuc'.

The same or another antiretroviral drug combination should be started as soon as possible. Never interrupt treatment if it can be avoided.

It is essential to stop all drugs and not just the one drug believed to be causing a problem.

NOTE Planned drug interruptions at regular intervals are not being used in the treatment of HIV.

Side effects of antiretroviral agents

5-69 What should be done if the patient has a severe reaction to a drug?

All drugs must be stopped immediately. *Never* stop only one drug. The whole drug combination must be assessed. Either of the following may be done:

1. All three drugs can be changed to another combination.
2. The drug causing the problem can be swapped, usually to a drug from another class as often there are similar side effects to other drugs in a the same class. For example, do not swap efavirenz for nevirapine. Rather replace nevirapine with lopinavir/ritonavir.
3. All drug side effects should be reported.

Immune Reconstitution Inflammatory Syndrome (IRIS)

5-70 What is the immune reconstitution inflammatory syndrome?

This is an unexpected clinical deterioration which occurs soon after antiretroviral treatment is begun. Functional immune recovery starts within weeks of beginning antiretroviral treatment. An inflammatory response to HIV-associated infections was not possible before antiretroviral treatment was started as the immune system was too suppressed. As the immune system recovers, the body may develop an inflammatory response to any of the following:

1. Hidden or mild infections which have been missed clinically (i.e. unmask unrecognised infection). An example would be silent TB.
2. Worsen existing infections. An example would be TB which has only been treated for a few weeks.
3. Infections which have been treated but antigens still remain. An example would be dead TB bacteria still present after a few months of anti-tuberculous treatment.

5-71 How many patients develop the immune reconstitution inflammatory syndrome?

Up to a third of patients starting antiretroviral treatment develop a mild immune reconstitution syndrome which does not require treatment. Rarely the immune reconstitution syndrome is serious and very rarely may be life threatening.

5-72 How does the immune reconstitutional inflammatory syndrome present clinically?

It usually presents with fever and a worsening of the patient's symptoms after starting antiretroviral treatment. All cases of possible immune reconstitution inflammatory syndrome must be urgently referred to an antiretroviral clinic. The immune reconstitution inflammatory syndrome usually presents abruptly within a month after antiretroviral treatment is started. Consider immune reconstitution inflammatory syndrome in anyone who is not thriving after six weeks of antiretroviral treatment.

The immune reconstitution inflammatory syndrome presents suddenly and unexpectedly with clinical deterioration in the patient's condition soon after antiretroviral treatment is started.

5-73 Which patients are most likely to develop the immune reconstitution inflammatory syndrome?

Patients with a CD4 count below 50 cells/µl when antiretroviral treatment is started.

5-74 What is the commonest cause of the immune reconstitution inflammatory syndrome in South Africa?

Tuberculosis is the commonest cause of the immune reconstitution syndrome in South Africa. The immune reconstitution inflammatory syndrome presenting with TB is less common if TB is treated for at least a month before starting antiretroviral treatment. Immune reconstitution inflammatory syndrome is not caused by treatment failure, side effects or drug interactions.

NOTE When starting antiretroviral treatment, TB may present for the first time (previously missed clinically) or partially treated TB (no live bacteria but antigen still present) may flare up with an acute inflammatory reaction. Suddenly enlarged paratracheal nodes, pleural effusions or parenchymal lung disease may be seen on chest X-ray. Mycobacteria avium complex infection is the commonest cause of the immune reconstitution inflammatory syndrome in developed countries. Severe acne, cryptococcal meningitis, cytomegalovirus retinitis, extensive molluscum, viral hepatitis, shingles, genital herpes and Kaposi's sarcoma have also been described with the immune reconstitution inflammatory syndrome.

5-75 How is a patient with the immune reconstitution inflammatory syndrome best managed?

The disease causing the inflammation must be diagnosed and treated. Avoid stopping antiretroviral treatment if at all possible. The patient may need to be referred to an HIV specialist.

Immune reconstitution inflammatory syndrome is not an indication to stop antiretroviral treatment.

NOTE A short course of steroids may have a role in managing a severe reaction.

Quality of life

5-76 How may the quality of life be negatively affected by antiretroviral treatment?

Some patients become anxious and depressed despite a good response to treatment because they face a lifetime of taking drugs for a chronic disease. A similar problem is seen with patients suffering from other chronic medical conditions such as diabetes and epilepsy. These patients need additional counselling and support. This problem can usually be avoided by good preparation before treatment is started.

NOTE Unsafe sexual practices have been shown to decrease once antiretroviral treatment is started. Patients become more responsible.

Expense

5-77 Does the cost of drugs affect antiretroviral treatment?

Unfortunately some antiretroviral drugs are expensive. If the state does not provide a free service, patients have to buy their own drugs. Expense is one of the reasons that antiretroviral treatment is not made available to all patients who need it. It is hoped that more cheaper

generic drugs will be produced for poor countries.

Case study 1

A patient who is 'treatment ready' attends her first treatment visit. She is clinically well with a CD4 count of 146cells/µl and has a good understanding of the treatment but is concerned about side effects as she works as a locum nurse and sometimes does night duties.

1. What should be done at the first treatment (commencement) visit?

After a pill count (of co-trimoxazole) and meeting with the counsellor to discuss the importance of excellent adherence, a final assessment is made by a clinician. This is followed by a visit to the pharmacist to collect the first month's supply of medication.

2. What medication will be given?

Patients are almost always started on the first-line combination (3TC/FTC, TDF and either nevirapine or efavirenz). Co-trimoxazole prophylaxis will also be continued until the patients CD4 count is above 200cells/µl .

3. What choice would you make for this patient?

3TC, TDF and nevirapine. Most patients would start on a fixed dose combination tablet of TDF, FTC and efavirenz but as this patient does shift work, efavirenz is not the best option as it often causes drowsiness.

4. How often should patients be seen during the first four months of treatment?

Routine visits should occur at monthly intervals with an extra visit at two weeks for patients receiving nevirapine.

5. Why are patients on nevirapine seen at two weeks?

Because the dose of nevirapine should be started at 1 tablet once daily and increased to 1 tablet twice daily at two weeks.

6. What should be done at the routine follow up visits?

At the routine visits the patients are weighed and clinically examined. A history is taken for adherence, side effects or other problems and the patient is counselled. A pill count is done, routine blood samples are taken and one month's supply of medication is given.

Case study 2

A patient attends all his routine visits for the first four months. He feels well and all his symptoms and signs of illness gradually disappear. He has no side effects from the antiretroviral treatment.

1. When should he attend the next follow up visit?

At six months after starting treatment. However, he should immediately return to the antiretroviral treatment clinic if he experiences side effects or has other problems.

2. How often do patients collect their medication?

Every one to three months. These visits should be used to assess and promote excellent adherence.

3. How is the success or failure of treatment determined?

By measuring the CD4 count and viral load as well as finding out whether the clinical signs of HIV have disappeared.

4. When should the CD4 count and viral load be measured after starting antiretroviral treatment?

The viral load should be measured at four or six months after starting treatment. Completing the first viral load earlier allows time for an adherence intervention if the viral load is raised, potentially reducing the risk of resistance. The viral load should be undetectable if treatment is successful. The CD4 count should be measured after one year on treatment if the CD4 count at the start of treatment was greater than 200cells/µl . If the CD4 count at the start of treatment was less than 200cells/µl, it should be measured at 6 monthly intervals until it is above 200cells/µl on two occasions. This is to guide prophylactic treatment with co-trimoxazole or fluconazole, both of which are stopped when the CD4 count is above 200cells/µl.

5. What is the single best measure of treatment success?

An undetectable viral load.

6. How should this patient be managed after six months?

If the antiretroviral treatment has been successful the patient may be seen every three months. However, he should continue to collect his medication regularly. His CD4 count and viral load should be measured at one year on treatment and he should continue to have a viral load test every year.

Case study 3

A patient who was started on a first line regimen of TDF, FTC and efavirenz is still ill after antiretroviral treatment for six months. Her CD4 count remains below 200 cells/µl and her viral load is above 1000 copies/ml.

1. What is your diagnosis?

Possible antiretroviral treatment failure.

2. What is the commonest cause of treatment failure?

Poor adherence.

3. How should this patient be managed?

It is important to establish whether adherence has been excellent or poor. If adherence is poor, every effort must be made to improve it. The viral load should then be measured again after three months. If it remains high the patient has failed antiretroviral treatment and treatment should be stopped until the patient has been fully prepared to start a second line treatment regimen.

4. What should be done if adherence has been excellent?

If the viral load remains high in spite of excellent drug adherence, the patient should be switched to a second-line regimen of AZT, 3TC and Aluvia without interrupting treatment. The HIV is probably resistant to the first-line drugs.

5. When are the routine visits with second- line treatment?

The same as first-line treatment with visits every month until 4 months followed by a visit at six months and then every three months thereafter if treatment is successful.

6. What routine blood tests should be taken if patients are on second-line treatment?

Before treatment is started an Hb with differential (or a FBC), glucose, triglyceride and cholesterol tests are done for baseline values.

After treatment has been started a Hb and differential should be done at months one, two, three and six to screen for anaemia, which is a common side effect of AZT. Fasting glucose, cholesterol and triglyceride should be measured at three or four months. These tests screen for metabolic abnormalities caused by lopinavir/ritonavir (Alluvia).

NOTE Some guidelines also recommend annual fasting glucose, cholesterol and triglycerides for patients on Aluvia.

Case study 4

A patient on antiretroviral treatment admits to poor adherence. He is sent to the treatment counsellor to discuss the importance of excellent adherence.

1. What is the definition of poor adherence?

Taking less that 95% of doses. Even moderate adherence, when between 80 and 95% of doses are taken, is not satisfactory. The goal must be to take all doses at the correct time.

2. What is the danger of poor adherence?

Antiretroviral treatment is likely to fail and there is a high chance of HIV resistance to the antiretroviral drugs.

3. What can be done to help this patient remember to take his medication?

Link the time for the dose with a particular radio or TV programme or an activity, e.g. cleaning his teeth. An alarm clock can be used or a supporter could remind him or send a cell phone message.

4. Why is drug resistance a danger for a patient?

Because it restricts the choice of drugs which are likely to be effective. If both the first- and second-line combinations fail, antiretroviral treatment may have to be stopped and the patient given only supportive care.

5. What is the danger of drug resistance to the community?

It makes HIV more difficult to treat. Others may become infected with a strain of HIV resistant to one or more drugs. Therefore it is in the interest of the whole community that patients take their antiretroviral treatment correctly.

6. How is the risk of drug resistance reduced?

By excellent adherence and always using combinations of at least three antiretroviral drugs.

Case study 5

Three weeks after starting antiretroviral treatment a patient becomes unwell with fever and severe cough. The patient had been reasonably well during the weeks before starting treatment despite having a very low CD4 count.

1. What is the likely diagnosis?

Immune reconstitution inflammatory syndrome (IRIS). Patients with a very low CD4 count at the start of antiretroviral treatment are at high risk of this condition.

2. What is the commonest cause of this condition in South Africa?

Tuberculosis. With fever and cough this patient probably has the immune reconstitution inflammatory syndrome due to TB. This can sometimes be prevented if the TB treatment is started before starting antiretroviral treatment.

3. What is the immune reconstitution inflammatory syndrome?

This is an inflammatory reaction which develops when the patient's immune system starts to recover. Before treatment is started, the immune system is too suppressed (weakened) to respond to an infection such as TB. The treatment therefore 'unmasks' an infection that previously had been 'hidden'.

4. How should this condition be managed?

It usually gets better if antiretroviral treatment is continued provided that the underlying cause is also treated. Immune reconstitution inflammatory syndrome is not an indication to stop antiretroviral treatment.

5. How long can HIV patients survive on antiretroviral treatment?

Provided their adherence is excellent, they can remain well with a good quality of life for many years.

6. What may affect the quality of life in these patients on successful treatment?

The fact that they have a chronic illness and must remain on treatment for life. The price of antiretroviral drugs may also be high in the private sector. These difficulties should be discussed with the treatment counsellor.

Dosing for patients on first-line combination

Medicine	Timing of doses	Possible side-effects
1. TDF (Tenofovir)300mg daily	24 hours	Kidney damage
2. 3TC (lamivudine) 300mg daily or FTC (emtricitabine) 200mg daily	24 hours	Diarrhoea, headache
3. Efv (Efavirenz) 600 mg daily	24 hours	Skin rash (allergy), vivid dreams, dizziness, sleep changes in first four weeks
		Most side effects get better after one to two months of treatment
Where possible, prescribe as a fixed dose combination tablet of TDF, FTC and Efavirenz as a once daily tablet (e.g. Atripla or Odimune one tablet daily)		

Dosing for patients on second-line combination

If 1st line treatment was TDF, FTC or 3TC and Efavirenz or Nevirapine, prescribe:

Medicine	Timing of doses	Possible side-effects
1. AZT (Zidovudine) 300 mg twice daily	12 hours	Numbness or pain in the feet, abdominal pain, hepatitis, acidosis
2. 3TC 150mg twice daily	12 hours	Diarrhoea, headache
3. LPV/r (Lopinavir + ritonavir) 400/100 twice daily (Aluvia 2 tablets twice daily)	12 hours	Skin rash (allergy), hepatitis
		Most side effects get better after one to two months of treatment

If 1st line treatment was AZT or d4t, 3TC and Efavirenz or Nevirapine (i.e. old first line), prescribe:

Medicine	Timing of doses	Possible side-effects
1. TDF 300 mg once daily	24 hours	Kidney damage
2. 3TC 150mg twice daily	12 hours	Diarrhoea, headache
3. LPV/r (Lopinavir + ritonavir) 400/100mg twice daily (Aluvia 2 tablets twice daily)	12 hours	Skin rash (allergy), hepatitis
		Most side effects get better after one to two months of treatment

6

HIV-associated infections

Before you begin this unit, please take the corresponding test to assess your knowledge of the subject matter. You should redo the test after you've worked through the unit, to evaluate what you have learned.

Objectives

When you have completed this unit you should be able to:

- Define HIV-associated infections.
- List the common HIV-associated infections.
- Diagnose and manage most HIV-associated infections.
- Explain why tuberculosis is a common and important HIV-associated infection.
- Describe how tuberculosis presents in patients with HIV infection.
- Describe the management of patients with tuberculosis and HIV co-infection.

Common HIV-associated infections

6-1 What are HIV-associated infections?

HIV-associated infections (or opportunistic infections) are infections which are common in patients with HIV infection. They 'take the opportunity' of infecting and causing illness in patients with a weakened immune system.

HIV-associated infections are common in patients with a weakened immune system.

6-2 Which are the common HIV-associated infections?

The following infections are *uncommon* in HIV-negative people, but common in HIV-positive people:

1. Oral candidiasis (thrush)
2. Tuberculosis (TB)
3. Recurrent bacterial pneumonia
4. Shingles (Herpes zoster)
5. Severe, recurrent genital herpes
6. Severe, recurrent mouth ulcers

The following infections are *rare* in HIV-negative people and are AIDS-defining. This means that people who have these infections usually have HIV infection.

1. Oesophageal candidiasis
2. Pneumocystis pneumonia
3. Cryptococcal meningitis
4. Cerebral toxoplasmosis
5. Cytomegalovirus (CMV) retinitis

NOTE Less common HIV-associated infections include chronic diarrhoea

due to isosporiasis or cryptosporidiosis, non-tuberculosis mycobacteria and disseminated fungal infections.

6-3 Do HIV-associated infections always indicate that the patient has AIDS?

No, as many of the milder HIV-associated infections such as pulmonary TB or shingles may also be found in HIV-negative patients and patients with stage 1 to 3 HIV infections (i.e. not AIDS). These infections, however, should always alert one to the fact that the patient may have HIV infection. HIV-associated infections are therefore an important indicator for HIV counselling and screening.

6-4 What are AIDS-defining illnesses?

Clinical conditions that are so rare in people with a healthy immune system that they usually indicate that the person has AIDS (stage 4 HIV infection). AIDS-defining illnesses include:

1. Infections such as oesophageal candidiasis, extrapulmonary TB, cryptococcal meningitis and pneumocystis pneumonia.
2. Illnesses, other than infections, such as HIV wasting syndrome, Kaposi's sarcoma and non-Hodgkin's lymphoma.

Both infections and malignancies can be AIDS-defining illnesses.

NOTE A number of malignancies associated with AIDS have a viral cause.

6-5 Which patients are at high risk of contracting HIV-associated infections?

1. HIV-infected patients with moderately low CD4 counts (50 to 200 cells/μl) commonly get infections which are uncommon in people with a normal immune system, e.g. tuberculosis and pneumococcal pneumonia. However, some of the milder HIV-associated infections may occur in HIV patients with CD4 counts above 200 cells/μl.
2. HIV-infected patients with very low CD4 counts (below 50 cells/μl) commonly become infected with rare organisms such as Pneumocystis and Toxoplasma.

The lower the CD4 count, the higher the risk of getting an HIV-associated infection.

6-6 Can HIV-associated infections be prevented?

The best way of preventing most severe HIV-associated infections and TB is to start antiretroviral treatment in HIV patients when their CD4 count reaches 350 cells/μl. The risk of HIV-associated infections can also be reduced by:

1. Primary prophylaxis that prevents the HIV-associated infection from occurring. This is done for Pneumocystis and TB.
2. Secondary prophylaxis that prevents recurrences of HIV-associated infections which have already occurred. This is done for cryptococcal meningitis.

6-7 How does oral candidiasis present?

Oral candidiasis (also called thrush or moniliasis) occurs mostly in HIV patients with a CD4 count below 200 cells/µl. It is a Stage 3 disease and may indicate advanced immunodeficiency. The patient complains of a painful mouth and white patches are seen on the tongue, palate and inside the cheeks. White patches may also be seen in the pharynx (oropharyngeal candidiasis). HIV-infected women often have severe or repeated vulvovaginal candidiasis.

NOTE The diagnosis of oral Candida infection can be confirmed on microscopy when the fungal spores and hyphae (threads) can be seen.

Oral candidiasis in adults is often an early sign that the patient has HIV infection.

6-8 How is oral candidiasis treated?

Candidiasis of the mouth and pharynx can be treated with topical nystatin drops 1 ml every six hours. A patient may also suck amphotericin B lozenges and patients who do not respond may be treated with fluconazole 100 mg daily for seven days. Recurrences are common in patients who are not on ART.

6-9 What bacterial infections are common in HIV patients?

Most HIV patients are at an increased risk of serious or repeated bacterial infections such as:

1. Meningitis
2. Pneumonia
3. Diarrhoea

A wide range of bacteria may cause meningitis or pneumonia such as Pneumococcus, Haemophilis and Staphylococcus. These infections should be treated as for patients who are not HIV positive.

Prophylaxis with co-trimoxazole reduces the risk of many bacterial infections.

Common bacterial infections are often serious or recurrent in HIV patients.

6-10 What organisms may cause diarrhoea in HIV patients?

A number of organisms that do not cause problems in healthy people may cause chronic diarrhoea in HIV-infected patients. Examples are non-typhoid Salmonella, Cryptosporidium and Isospora. Patients with severe or chronic diarrhoea should be referred to hospital if dehydrated.

NOTE Isosporiasis responds to co-trimoxazole. Cryptosporidium infection often only resolves when the patient is given antiretroviral treatment.

6-11 What is shingles?

Shingles is a very painful vesicular rash which usually only affects one part of the body. It is commonly seen in older people and is uncommon in young healthy adults. It is caused by reactivation of the chickenpox virus

(Varicella zoster) which has been silent in nerve cells since a childhood infection. Shingles is infectious and can cause chickenpox in children. Pain typically occurs for a few days before the rash appears.

Shingles is common in young adults with HIV infection as their damaged immune system no longer keeps the virus under control. Patients with shingles should be treated early with high doses of oral acyclovir (800 mg 4-hourly for five days). The eye may become involved, which can cause blindness. Patients with face or eye involvement should be urgently referred to hospital for treatment.

Shingles in a young adult suggests HIV infection.

NOTE Early treatment with steroids and acyclovir may prevent the development of painful post-shingles neuralgia. Only use after consultation with an infectious-disease specialist.

6-12 Why is recurrent herpes infection common in HIV patients?

A painful, recurrent rash with many small vesicles in the genital or anal area is usually due to a Herpes simplex infection. This sexually transmitted disease is often severe and recurrent in patients with HIV infection due to their damaged immune systems. The mouth and lips may also be involved. Patients with severe infection should be treated with oral acyclovir (400 mg 8-hourly for five days).

Recurrent, severe herpes is common in HIV patients.

NOTE Genital and anal herpes are usually sexually transmitted and caused by Herpes simplex virus II (HSV-II) while oral herpes is usually due to recurrence of a childhood infection caused by HSV-I.

6-13 What are common causes of a sore mouth in HIV patients?

1. Oral candidiasis. This is the commonest mouth condition associated with HIV infection.
2. Severe, recurrent aphthous ulcers. These are very painful ulcers that can occur anywhere in the mouth. They may be single or multiple, small or large. Manage with paracetamol (Panado) for pain, and chlorhexidine mouthwashes to prevent secondary bacterial infection. Local (topical) steroids (e.g. Kenalog in Orabase) or spraying a beclomethasone inhaler directly onto the ulcer is helpful in severe cases.
3. Herpes infections. These multiple, shallow ulcers often are recurrent or become chronic. Topical gentian violet or 0.1% povidone-iodine (Betadine mouth wash) may be used while oral acyclovir is indicated for large ulcers.
4. Necrotising ulcerative gingivitis. This causes bleeding and ulceration along the gum margins of the teeth. Mouth washes with 0.2% chlorhexidine gluconate helps while oral metronidazole (Flagyl) is indicated in severe cases. Severe cases should be referred to a dental hygienist.

In contrast, oral hairy leucoplakia is not painful and does not require any treatment.

6-14 How does oesophageal candidiasis present?

Oesophageal candidiasis is very common in patients with a CD4 count below 100 cells/μl. Patients present with pain and difficulty on swallowing. Patients with oesophageal candidiasis usually have oral candidiasis as well, which helps make the diagnosis. Oesophageal candidiasis may result in dehydration due to poor fluid intake.

Oesophageal candidiasis presents with painful swallowing and almost always indicates advanced HIV infection.

6-15 How is oesophageal candidiasis treated?

Oesophageal candidiasis is treated with oral fluconazole (200 mg daily for 14 days). Local treatment with topical drugs is not adequate. Patients with oesophageal candidiasis must be referred to hospital if they need intravenous rehydration. It is useful to give patients a glass of water to drink so that you can assess how easily they are able to swallow.

Pneumocystis pneumonia

6-16 What is pneumocystis pneumonia?

Pneumocystis pneumonia is a severe lung infection caused by a fungus called Pneumocystis. HIV patients, especially children, are particularly likely to develop pneumocystis pneumonia if their CD4 count is below 100 cells/μl.

NOTE Contrary to earlier teaching, Pneumocystis jiroveci and not Pneumocystis carinii infects humans. Pneumocystis has recently been identified as a fungus.

6-17 How is pneumocystis pneumonia diagnosed?

The patient presents with:

1. Fever
2. A dry cough
3. Shortness of breath, especially with exercise
4. Weight loss, fatigue and a feeling of being unwell
5. Cyanosis in severe cases

Early in the infection the chest X-ray may appear normal. Later the appearance is that of 'ground glass', often involving both lungs.

NOTE A definitive diagnosis is made by staining sputum, which can be obtained after saline nebulisation in a patient with a dry cough. Treatment may be initiated in patients with clinical symptoms after tuberculosis and bacterial pneumonia have been excluded.

6-18 How is a patient with pneumocystis pneumonia managed?

Oral co-trimoxazole, four tablets every six hours in patients of 60 kg or more and three tablets every six hours in patients under 60 kg, is the treatment of choice. Severe cases also require steroids. Patients with severe pneumonia need to be hospitalised, and will need oxygen.

NOTE The full blood count with differential, neutrophil count and serum potassium concentration should be monitored in patients on such high doses of co-trimoxazole.

6-19 Can pneumocystis pneumonia be prevented?

Yes. Prophylactic oral co-trimoxazole, two tablets daily should be given to HIV-infected patients with a CD4 count below 200 cells/µl or stage 2, 3 or 4 disease. Prophylaxis can be stopped when the CD4 count is above 200 cells/µl after starting treatment.

NOTE Dapsone 100 mg daily can be used by patients who do not tolerate co-trimoxazole.

6-20 Can prophylactic co-trimoxazole prevent other HIV-associated infections?

Prophylactic co-trimoxazole can lower the risk of the following HIV-associated infections:

1. Pneumocystis pneumonia
2. Toxoplasmosis
3. Bacterial infections
4. Diarrhoea caused by Isospora

NOTE Dapsone only prevents Pneumocystis infections.

6-21 Does co-trimoxazole have side effects?

Yes. Especially in patients who are receiving antiretroviral treatment. The commonest side effect is a rash. This can be severe and even life threatening. The rash can occur for the first time even if the patient has been on co-trimoxazole treatment for many months or years.

NOTE Co-trimoxazole may cause hypersensitivity reactions with bone marrow suppression as well as hepatitis.

Infections of the central nervous system

6-22 Which HIV-associated infections can affect the brain?

1. Cryptococcal meningitis
2. Toxoplasmosis
3. Cytomegalovirus (CMV)
4. Tuberculous meningitis

6-23 What is cryptococcal meningitis?

This is a serious infection of the meninges caused by a fungus called Cryptococcus neoformans. Cryptococcal meningitis is rare in healthy people and is not infectious to others. It is usually seen in patients with advanced HIV infection and a CD4 count below 100 cell/µl.

Cryptococcus is an important cause of meningitis in patients with advanced HIV infection.

NOTE Cryptococcus may also cause a disseminated infection which involves other organs such as the lungs and skin.

6-24 How is cryptococcal meningitis diagnosed?

It presents with the clinical signs of meningitis, i.e. fever, headache, nausea and vomiting, neck stiffness, confusion and drowsiness.

The diagnosis is confirmed by examining the cerebrospinal fluid (CSF) obtained by lumbar puncture. The diagnostic tests on the CSF are:

1. Indian ink stain
2. Cryptococcal antigen
3. Culture

NOTE CSF chemistry may be normal or only mildly abnormal early in the infection. The Indian ink stain is not very sensitive while culture takes weeks. The antigen test in both CSF and serum is very sensitive for cryptococcal meningitis.

6-25 How is cryptococcal meningitis treated?

All patients with a clinical suspicion of meningitis must be urgently referred to hospital. Amphotericin B is given intravenously for two weeks followed by high oral doses of fluconazole for a further eight weeks.

6-26 Can cryptococcal meningitis be prevented?

Yes. Patients with CD4 counts below 100 cells/µl should have blood taken for a cryptococcal latex agglutination test (CLAT) and if positive and asymptomatic, should receive primary prophylaxis with fluconazole. The dose for primary prophylaxis is 800mg fluconazole by mouth daily for 2 weeks, then 400mg daily by mouth for 8 weeks, then 200mg per day until the CD4 count is above 200cells/µl for at least 6 months.

Patients who have been treated and have recovered from cryptococcal meningitis should be placed on secondary fluconazole prophylaxis to reduce the risk of a repeat infection. The dose of daily oral fluconazole for secondary prophylaxis is 200 mg daily. Prophylaxis can be stopped when the CD4 count rises above 200 cells/µl.

NOTE Fluconazole is used both as primary prophylaxis for the prevention of cryptococcal meningitis and as secondary prophylaxis to prevent a recurrence after treatment of cryptococcal meningitis..

6-27 What is cerebral toxoplasmosis?

Toxoplasma gondii is a single-cell organism (parasite) that can cause serious illness with brain infection (encephalitis) in patients with advanced HIV infection and a CD4 count below 100 cells/µl. Toxoplasmosis is not infectious to others. Patients with cerebral toxoplasmosis present with fits, abnormal behaviour and/or drowsiness. The diagnosis is confirmed on CT scan. Patients with suspected cerebral toxoplasmosis must be urgently referred to hospital for investigation and treatment with a prolonged course of co-trimoxazole.

Cerebral toxoplasmosis is a serious complication of AIDS.

6-28 What problems may be caused by cytomegalovirus (CMV)?

This virus commonly causes mild illness in healthy children and adults. Most people are infected as children. In HIV-infected patients with a very low CD4 count, CMV may cause retinitis (infection of the eye), encephalitis (brain infection), hepatitis, pneumonitis and bowel infection. This may be a primary infection or recurrence of a childhood infection.

CMV retinitis presents with sudden impaired vision and is the commonest cause of blindness in HIV patients with low CD4 counts. Suspected cases must be urgently referred to hospital for diagnosis and treatment with ganciclovir. Visual impairment caused by CMV may be permanent.

CMV retinitis may cause blindness in HIV patients.

Tuberculosis co-infection

6-29 What is tuberculosis co-infection?

Tuberculosis co-infection occurs when the patient has tuberculosis and HIV infection at the same time.

6-30 What is tuberculosis?

Tuberculosis (TB) is a chronic infectious disease which is caused by TB bacteria. Tuberculosis disease usually affects the lungs (pulmonary tuberculosis), but may involve other organs (extrapulmonary tuberculosis).

NOTE: Mycobacterium tuberculosis, the common cause of tuberculosis, was first described by Robert Koch in 1882. Non-tuberculous Mycobacterial infections such as Mycobacterium avium complex (or MAC) may occur in patients with advanced HIV infection.

6-31 How are TB bacteria spread from person to person?

TB bacteria are usually spread when a person with untreated pulmonary tuberculosis talks, coughs, spits, laughs, shouts, sings or sneezes. This sends a spray of very small droplets into the air. These small drops contain live TB bacteria (TB bacilli) from the person's lungs. They float in the air for up to one hour and can be breathed in by other people. This may result in TB infection of the lung. Patients with many TB bacteria in their sputum ('open TB') are very infectious to others.

NOTE Less commonly, TB bacteria in unpasteurised cows' milk can be drunk and cause TB infection of the intestines.

TB bacteria are spread by people with untreated pulmonary tuberculosis.

6-32 Do all people who are infected with TB bacteria develop tuberculosis?

No. Most people infected with TB bacteria do not develop tuberculosis because their healthy immune system

is able to control the infection and stop the TB bacteria from multiplying and spreading. However, the TB bacteria are often not all killed but only kept under control. The normal immune response in people without HIV infection prevents the TB infection from progressing to tuberculosis (TB disease).

Fortunately most HIV-negative people infected with TB bacteria do not develop tuberculosis.

6-33 How soon after TB infection does tuberculosis develop?

This will depend on the ability of the person's immune system to control the spread of the TB bacteria. If the immune system is strong the TB infection will be well controlled and not spread to other parts of the lung or to other organs (primary infection only, without progressing to tuberculosis). However, if the immune system is weak, the TB infection may rapidly spread within the lung or to other organs (tuberculosis or TB disease). Some patients are able to control the primary infection for months or many years (latent phase) but the infection may then spread to cause tuberculosis if the immune system becomes weakened (reactivation).

6-34 Is TB infection common in the general population in South Africa?

Infection with TB bacteria is very common, and it is estimated that almost 50% of all South Africans are infected, especially during childhood. However, only about 10% of healthy, HIV-negative people with TB infection develop tuberculosis disease during their lifetime. Therefore, TB infection is far more common than tuberculosis in the general population.

TB infection is very common in South Africa.

6-35 Are patients with HIV infection at increased risk of developing tuberculosis?

Yes. Tuberculosis is very common in people with HIV infection, and is often the first indication of illness in a person who is HIV positive. All patients with HIV infection are at an increased risk of developing tuberculosis because of their suppressed immune system. In HIV-positive people, new primary TB infection progresses to tuberculosis in 30% of cases, while an additional 10% per year will develop tuberculosis disease due to reactivation of an old latent TB infection. This contrasts with HIV-negative people who only have a small risk of developing tuberculosis in their lifetime. HIV has therefore changed the natural history of tuberculosis, making it the most common HIV-associated infection in South Africa.

Tuberculosis is very common in HIV-positive people and is the most common HIV-associated infection in South Africa.

6-36 How many adults with tuberculosis also have HIV infection?

In South Africa over 50% of adults with tuberculosis are also HIV positive. It is therefore essential to screen for HIV in all patients presenting with tuberculosis.

All patients with tuberculosis must be screened for HIV infection.

6-37 Why is tuberculosis so common in patients with HIV infection?

HIV-positive patients have damaged immune systems which are not able to control the TB infection. Tuberculosis in HIV-positive people may be due to either:

1. Reactivation of a latent TB infection, which has been under control for many years. Often the original TB infection occurred during childhood. With weakening of the immune system by HIV infection the old TB infection starts to spread, resulting in tuberculosis.
2. A new primary TB infection which progresses to tuberculosis. The weakened immune system is unable to kill the TB bacteria and keep the TB infection under control.

HIV infection probably does not increase the risk of TB *infection* but greatly increase the risk of old or new TB infections progressing rapidly to tuberculosis.

6-38 What is the effect of HIV infection on the progress of tuberculosis?

The course of tuberculosis is often very rapid in patients with HIV infection. Both new and old TB infections spread quickly. Therefore, patients with both HIV infection and tuberculosis may need hospitalisation.

The course of tuberculosis is very rapid in patients with HIV infection.

NOTE HIV infection with a damaged immune system prevents the normal cellular response to TB.

6-39 Is tuberculosis a common cause of death in people with HIV infection?

Tuberculosis is the most common cause of death in adults with HIV infection in South Africa.

Tuberculosis is the commonest cause of death in adults with HIV infection in South Africa.

6-40 What is the effect of tuberculosis on the progress of HIV infection?

Patients with untreated HIV infection become worse much more rapidly if they also have TB co-infection, which further damages the immune system.

Therefore, HIV infection speeds up the progress of tuberculosis while

tuberculosis speeds up the progress of HIV infection. This is the great danger of HIV/TB co-infection.

The progress of HIV infection is made worse with TB co-infection.

6-41 Which organs, other than the lungs, can be affected by tuberculosis?

Tuberculosis may affect most organs of the body, such as the lymph nodes, bowel, meninges, brain, kidneys and spine, especially in people with HIV infection. This is called extrapulmonary tuberculosis. The commonest form of extrapulmonary tuberculosis in HIV-positive people is enlarged lymph nodes (tuberculous lymphadenopathy). Tuberculous meningitis and disseminated tuberculosis are also common in HIV-infected patients. Disseminated tuberculosis presents with two or more organs involved.

The risk of extrapulmonary tuberculosis increases when the CD4 count is low. Therefore, extrapulmonary tuberculosis is more common in people with advanced HIV disease.

6-42 What are the symptoms and signs of pulmonary tuberculosis?

Patients with pulmonary TB may present with any of the following:

1. Chronic cough for more than two weeks. Some patients may cough up blood (haemoptysis).
2. Fever for more than two weeks.
3. Severe night sweats for more than two weeks.
4. Weight loss.
5. Tiredness and weakness.

A careful history is the best way to screen for tuberculosis. Any two of the above symptoms or signs strongly suggests tuberculosis. Always suspect tuberculosis in any HIV-positive person who has a cough lasting more than two weeks. Advanced HIV infection can also result in fever, night sweats, weight loss, tiredness and weakness.

Pulmonary tuberculosis usually presents with chronic cough, fever, severe night sweats and weight loss.

6-43 How is the clinical diagnosis of pulmonary tuberculosis confirmed?

1. Two sputum samples should be sent for testing for acid-fast bacilli (i.e. TB bacteria). If available, a GeneXpert test should be done. GeneXpert is a rapid and sensitivemethod of detecting TB bacilli in sputum. It can also determine if the TB bacilli are resistant to rifampicin. If the GeneXpert or smear result is positive, the patient should be started on TB treatment.

Smear-positive patients have pulmonary tuberculosis and are infectious.

2. If the GeneXpert or smear is negative, the second specimen should be used for TB culture.
3. Patients who have clinical findings that are very suggestive

of pulmonary TB but a negative GeneXpert or smear should have a chest X-ray if possible. This is particularly important for sick patients with low CD4 counts as the delay in making the TB diagnosis while waiting for a TB culture result could be fatal. Typical adult tuberculosis with cavities (holes) in the upper lobes may be seen in patients with only mild depression of their CD4 count. However, patients with advanced HIV infection may have widespread TB pneumonia, pleural effusions or enlarged TB lymph nodes (non-cavity tuberculosis).

4. A sputum culture should be done in all HIV-positive patients with symptoms of TB and a negative smear or GeneXpert result. The culture may be positive even if the smear examination is negative.
5. In HIV-positive patients with tuberculosis, the chest X-ray may appear normal and the GeneXpert or sputum stain and culture may also be normal, making the clinical diagnosis difficult to confirm. A good clinical response to TB (anti-tuberculous) treatment may be the only way to confirm the diagnosis in these patients.

Sometimes the clinical diagnosis of tuberculosis is difficult to confirm.

NOTE Lymph node biopsy is often helpful. Ideally all positive sputum samples should be cultured for drug resistance.

6-44 Are HIV patients with pulmonary tuberculosis a danger to the general public?

Any patient with pulmonary tuberculosis may be infectious to the general public. As the number of HIV patients with tuberculosis increases, the risk of tuberculosis in HIV-negative people will also increase as they are being exposed to more TB bacteria. As a result of the HIV epidemic, tuberculosis has become a common disease in South Africa. It is therefore in the public's best interest to prevent and manage tuberculosis well.

The HIV epidemic is increasing the risk of tuberculosis to the general public.

NOTE In South Africa the steady fall in numbers of tuberculosis cases suddenly reversed in the 1990s when the incidence of tuberculosis dramatically climbed as the HIV epidemic spread.

6-45 How can tuberculosis be prevented in patients with HIV infection?

1. The risk of tuberculosis can be reduced in HIV-positive people by controlling tuberculosis in the general public and thereby reducing their exposure to TB bacteria. A high cure rate of tuberculosis by a well-functioning DOT programme is very important.
2. Some protection can be obtained by giving all children BCG immunisation at birth.

3. INH prophylaxis can be given to patients at high risk of tuberculosis.

6-46 What does DOT stand for?

Directly Observed Therapy (DOT) is a course of TB treatment where taking the medication is observed each day by a supporter. The supporter is a responsible friend or family member or a healthcare worker who makes sure that each dose of TB treatment is correctly taken.

NOTE In contrast, DOTS (Directly Observed Therapy Shortcourse) is a management programme which uses a short, intensive course of TB treatment that is supervised by a supporter.

6-47 What is TB prophylaxis?

HIV-infected patients at high risk of tuberculosis can be protected by isoniazid (INH) at a dose of 300 mg daily. Prophylaxis prevents the reactivation of an old TB infection as well as the spread of new TB infections.

It is suggested that TB prophylaxis should be given to HIV-positive patients who have a positive Mantoux skin test result of 5 mm or more. A positive Mantoux skin test indicates that the person has previously had TB infection. INH prophylaxis should be given for at least 36 months, It is very important to exclude active tuberculosis before starting INH prophylaxis as monotherapy with INH may lead to TB drug resistance.

TB prophylaxis is important in HIV-infected people at high risk of tuberculosis.

NOTE Pyridoxine 25 mg per day is often given with INH to reduce the risk of INH-induced peripheral neuropathy.

6-48 Should HIV infection and tuberculosis be treated at the same time?

Yes. However, the TB treatment should be started before beginning antiretroviral treatment because:

1. The immune reconstitution inflammatory syndrome (IRIS) may occur. This is particularly common if TB treatment is given for less than two months before antiretroviral treatment is started, especially if the CD4 count is less than 50 cells/μl.
2. Adverse effects due to interactions between the various anti-tuberculosis and antiretroviral drugs are common.
3. TB and antiretroviral drugs often have similar side effects, which can be more frequent and severe if the drugs are taken together.
4. A large number of different tablets have to be taken when both infections are treated at the same time. This may affect adherence.

Therefore treatment of HIV and tuberculosis at the same time has many problems. However, if antiretroviral treatment is delayed too long, the patient may become seriously ill or die.

Tuberculosis treatment should be started before starting antiretroviral treatment.

6-49 How is drug-sensitive tuberculosis treated?

An intensive phase of treatment for two months is followed by a continuation phase of four months. Therefore, treatment for tuberculosis usually lasts six months.

Usually rifampicin, isoniazid (INH), pyrazinamide and ethambutol are given in a combination tablet for the intensive phase of treatment. Daily dosage with combination tablets is given according to body weight:

- 2 tablets for patients weighing 30 to 37 kg
- 3 tablets if 38 to 54 kg
- 4 tablets if 55 to 70 kg
- 5 tablets if over 70 kg

For the continuation phase, a combination tablet of rifampicin and INH only is used:

- 2 tablets for patients weighing 30 to 37 kg
- 3 tablets if 38 to 54 kg
- 4 tablets if 55 kg or more.

Tuberculosis in patients with HIV infection usually responds well to treatment.

The commonly used combination tablet for the intensive phase contains rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg and ethambutol 275 mg, while the combination tablet for the continuation phase contains rifampicin 150 mg and isoniazid 75 mg. Double-strength tablets are available for patients weighing 55 kg or more

Tuberculosis is treated with a multiple drug regimen using combination tablets.

6-50 What is the importance of excellent adherence to treatment?

As with antiretroviral treatment, it is extremely important that TB treatment is given correctly every day for the full course. Poor adherence is the main reason for treatment failure and an important cause of drug-resistant tuberculosis.

6-51 Do HIV patients on antiretroviral treatment have a lower risk of tuberculosis?

The risk of tuberculosis is greatly reduced in the short term in patients on antiretroviral treatment (in the first three years) as their CD4 counts are increasing. However, as patients on antiretroviral treatment now live longer, the lifetime risk of TB is still high. As a result, the incidence of tuberculosis in the community may not fall with the roll-out of antiretroviral treatment.

6-52 Is it important to screen all patients for tuberculosis before starting antiretroviral treatment?

Yes. Tuberculosis should be excluded by taking a careful history before starting antiretroviral treatment. Any HIV patient with a chronic cough should be fully investigated for tuberculosis.

6-53 When should antiretroviral treatment be started in HIV-positive patients who have tuberculosis?

1. Start ART between 2 to 10 weeks after starting TB treatment if:
   - the CD4 count is above100 cells/µl and the patient is well
   - the patient, does not have Stage 4 disease the patient does not haver markers of severity (low BMI or low haemoglobin level).
2. Start ART after two weeks of TB treatment if:
   - the CD4 count is below 100 cells/µl
   - clinical stage is 4
   - the patient is severely ill
   - the patient may die if the treatment is delayed any longer.
3. Patients with TB meningitis (or cryptococcal meningitis) should have TB treatment for 4 to 6 weeks before starting ART.

6-54 What should be done if patients on antiretroviral treatment develop tuberculosis?

The antiretroviral treatment must be continued and TB treatment started. There is no need to delay starting the TB treatment.

6-55 How do drugs used to treat tuberculosis and HIV interact with each other?

In patients who are already on antiretroviral treatment when tuberculosis is diagnosed, some of the drugs being used in antiretroviral treatment may have to be changed:

1. Rifampicin is very important in the treatment of tuberculosis but it affects the serum drug levels of many of the drugs used in antiretroviral treatment. As a result, the choice of antiretroviral drugs and their doses may need to be changed.
2. If the first-line combination is to be used, nevirapine is often replaced with efavirenz as rifampicin may lower the blood level of nevirapine. There is also an increased risk of liver toxicity if nevirapine and TB medication are used together.
3. If the second-line antiretroviral combination is to be used, the dose of lopinavir/ritonavir should be doubled (from 2 Aluvia tablets twice daily. to 4 Aluvia tablets twice daily.), as TB treatment lowers the blood level of lopinavir.

As there are complex interactions between the drugs used to treat TB and the drugs used for antiretroviral treatment, the management of these patients may need to be reviewed by a doctor experienced in managing patients with TB/HIV co-infection.

NOTE: Tenofovir should not be used with aminoglycosides as both are potentially nephrotoxic. Patients with drug resistant TB who require an aminoglycoside should preferably not be treated with Tenofovir. AZT (Zidovudine) may be used instead.

Drugs used in TB therapy and antiretroviral treatment may interact with each other.

NOTE Rifampicin induces liver enzymes which break down some drugs used in antiretroviral treatment.

6-56 What are the shared side effects of the drugs used to treat tuberculosis and HIV?

Nausea, rash, hepatitis and peripheral neuropathy may be caused by both the drugs used to treat tuberculosis and those to treat HIV. As a result these side effects (adverse effects) are commoner and may be more serious if the two drug regimens are used together. This may result in a change in the choice of antiretroviral drugs.

Drug side effects are more frequent and may be more severe if anti-tuberculous and antiretroviral treatments are given together.

6-57 Can taking many tablets at a time cause problems?

Adherence may be poor when so many tablets need to be taken together. There may also be confusion between the many different types of tablets. Patients should be told they will have to take a large number of tablets and be counselled about these possible problems. A clearly written plan for both TB and antiretroviral treatment is helpful.

6-58 Is resistant tuberculosis a problem in HIV patients?

Tuberculosis resistant to many of the TB drugs is a growing problem in both HIV-positive and negative people. A combination of HIV infection and drug-resistant tuberculosis is often fatal. Therefore, good adherence is essential in the treatment of both tuberculosis and HIV to prevent drug resistance.

Multi-drug-resistant (MDR) TB is resistant to both INH and rifampicin. This is becoming a worry in South Africa.

NOTE Extensively drug-resistant (XDR) TB is resistant to more than INH and rifampicin and often resistant to all the standard TB drugs.

6-59 Are the public health strategies to treat tuberculosis and HIV similar?

There are important differences in the way that treatment is managed:

1. In TB programmes that use the DOTS approach, responsibility for ensuring adherence is largely placed on a supporter rather than on the patient. In contrast, with antiretroviral treatment, the responsibility is on patients themselves.
2. A course of TB treatment is usually for six to eight months only, while antiretroviral treatment is for life.

6-60 Who should be responsible for the TB treatment?

Previously HIV patients with tuberculosis co-infection were referred to a local TB clinic for treatment of their tuberculosis. This is unsatisfactory and HIV and TB infections should preferably be managed at a single clinic.

Patients with TB/HIV co-infection should be managed at a single clinic.

6-61 What are the advantages of managing both tuberculosis and HIV at the same clinic?

- It avoids the need for referring patients to a separate clinic for their TB treatment. Previously the need to attend two clinics, often far apart from each other, was inconvenient for patients, with the result that many did not attend clinic regularly. This resulted in poor adherence and more drug resistance. It also added to the cost of transport and resulted in more days away from work.
- Doctors and nurses managing patients with HIV infection in one clinic also found it difficult to know what other treatment the patient was receiving at another clinic and how the patient was responding to treatment. With a combined clinic, the patients only need to get to know one set of staff which improved communication.
- As the adverse effects of antiretroviral drugs and TB drugs are often similar and more severe, and there may be drug interactions, it is far better if the management of both conditions is managed by a single team of health workers.
- With a combined HIV/TB clinic fewer HIV-positive patients should die of undetected tuberculosis.

There are many advantages to the combined management of tuberculosis and HIV infection.

6-62 How can adherence to TB treatment be improved?

- Use Directly Observed Therapy (DOT) or Community Care Worker support for home treatment.
- Treatment counselling should be given to teach the importance of excellent adherence and prepare for home treatment. Usually three counselling sessions are given by a treatment counsellor at the health facility.
- Treatment should be started and supervised at the health facility for two weeks while the patient is being counselled. This also allows for any adverse effects to be detected.
- Arrange a home visit by communuty care worker to identify any factors which may increase the risk of poor adherence or stopping treatment.
- The patient should identify a suitable treatment supporter (treatment 'buddy') who can assist with DOT and report any treatment problems. The treatment supporter should attend at least one, and preferably all three counselling sessions at the health facility.
- Further treatment sessions are given at the start of the continuation phase.

If all these steps are taken treatment adherence should be excellent and most patients should complete their full course of treatment. This will improve survival and reduce the risk of drug resistance.

Case study 1

A 20-year-old man presents with a very painful mouth for the past few days. On examination he has white patches on his tongue and palate. When questioned, he admits to difficulty swallowing.

1. What is the likely diagnosis?

Oral candidiasis. He probably also has oesophageal candidiasis as he has difficulty swallowing.

2. What is the likely underlying cause?

HIV infection with suppression of his immune function. Oral candidiasis is uncommon in healthy adults with a normal immune system.

3. What is the management of oral candidiasis?

Topical nystatin drops 1 ml every six hours. He could also suck amphotericin B lozenges or nystatin vaginal pessaries. Prescribe oral fluconazole or refer if the candidiasis is not cleared after five days of treatment.

4. What is the management of oesophageal candidiasis?

Oral fluconazole. Make sure the patient is not dehydrated. If so, intravenous fluid may be needed. Dehydrated patients should be referred to hospital.

5. What are the other causes of a sore mouth in a patient with HIV infection?

Aphthous ulcers, herpes ulcers and gingivitis.

6. Is oral candidiasis an HIV-associated infection?

Yes. An HIV-associated infection occurs far more commonly in HIV-positive people than people who are HIV negative. These infections are more common because HIV damages the immune system by reducing the CD4 count. Oral candidiasis indicates stage 3 disease.

Case study 2

A young woman complains of weight loss and chronic diarrhoea. For the past few days she has had severe pain on one side of her chest. She has noticed a rash with small vesicles (blisters) in the same area as the pain.

1. What is the cause of the pain and rash?

Herpes Zoster (Shingles). This typically presents as localised pain followed by a vesicular rash.

2. Is this the same as chickenpox?

No, but both rashes are due to the Varicella zoster virus. For many years the virus remains in nerve cells following chickenpox as a child. When the immune system is weakened, the virus is reactivated, causing shingles. Shingles is infectious and can cause chickenpox in others.

3. What is the concern when a young person gets shingles?

It suggests that the person has HIV infection. Shingles is uncommon in healthy HIV-negative young people and is usually seen in an older person.

4. What is the management of shingles?

Early treatment with oral acyclovir. If the pain or rash involves the face or eye, the patient must be referred urgently to hospital.

5. What is the likely cause of her chronic diarrhoea?

This is almost certainly caused by an infection associated with HIV. A number of organisms cause chronic diarrhoea in HIV patients, such as non-typhoid Salmonella, Cryptosporidium and Isospora. She should be treated symptomatically and a stool sample should be sent for microscopy and culture. If the diarrhoea does not resolve despite treatment and ART, she should be referred to hospital for further diagnosis and treatment.

6. What prophylaxis will help prevent chronic diarrhoea?

Prophylaxis with co-trimoxazole will help prevent diarrhoea due to bacterial infections as well as infections with Isospora.

Case study 3

A known HIV patient develops a dry cough and fever. After a few days he feels worse and becomes short of breath.

1. What is the probable diagnosis?

Pneumonia. Cough, fever and shortness of breath suggest a lung infection.

2. What are the likely causes?

Bacterial pneumonia, pneumocystis pneumonia or tuberculosis. The most likely cause is pneumocystis pneumonia.

3. How can the diagnosis be confirmed?

A chest X-ray will be helpful in most cases. Exclude tuberculosis and bacterial pneumonia. Where laboratory support and saline nebulization are available, request an examination for Pneumocystis in a sputum specimen.

4. What is the treatment of pneumocystis pneumonia?

Oral co-trimoxazole, four tablets every six hours in patients weighing 60 kg or more and three tablets every six hours in patients under 60 kg. Patients who are severely ill or cyanosed need oxygen and admission to hospital. Severe cases may need steroids.

5. What is an AIDS-defining illness?

These are conditions which are very rare in people who do not have AIDS (stage 4 HIV infection). Pneumocystis is an AIDS-defining illness, therefore anyone presenting with pneumocystis pneumonia almost certainly has AIDS. Certain malignancies such as Kaposi's

sarcoma and non-lymphoid lymphoma are also AIDS-defining illnesses.

6. What other infections are AIDS-defining illnesses?

Oesophageal candidiasis, cryptococcal meningitis, cerebral toxoplasmosis and CMV retinitis all indicate stage 4 HIV infection.

Case study 4

An HIV-positive patient presents with a chronic cough, night sweats and fever. A chest X-ray suggests pulmonary tuberculosis.

1. How common is tuberculosis in HIV-positive patients?

Very common. It is the commonest HIV-associated infection in adults in South Africa.

2. Is tuberculosis dangerous in patients with HIV?

Yes, it is the commonest cause of death in adults with HIV in South Africa.

3. How can tuberculosis be prevented in HIV-positive people?

Controlling tuberculosis in the general population and the routine use of BCG immunisation in infants. TB prophylaxis (primary prevention) with isoniazid in HIV patients with a positive Mantoux skin test is effective in reducing the incidence of tuberculosis in these high-risk patients.

4. How is tuberculosis treated?

With a course of multi-drug therapy. Usually rifampicin, isoniazid, pyrazinamide and ethambutol are used together. HIV-positive patients with tuberculosis usually respond well to TB treatment.

5. Should tuberculosis and HIV both be treated at the same time?

If possible, TB treatment should be started first before starting antiretroviral treatment. Therefore all patients should be screened for tuberculosis before antiretroviral treatment is started. If the patient is already on antiretroviral treatment when the diagnosis of tuberculosis is made, the anti-tuberculosis treatment should be added to the antiretroviral treatment without delay.

6. What are the problems if tuberculosis and HIV are treated together?

Drugs used to treat tuberculosis and HIV often interact with each other. The risk of side effects is increased and adherence is often poor due to the large number of tablets that have to be taken each day.

6A

Skills workshop: Screening tests for HIV

Objectives

When you have completed this unit you should be able to:

- Screen a patient for HIV.
- Interpret the results of the screening test.

Whenever possible, patients should be offered and encouraged to accept screening for HIV. An HIV rapid test can be used in any clinic, as no sophisticated equipment is required. Prior to testing, patients need to be counselled and consent must be obtained.

A. Equipment needed to perform an HIV rapid test

1. The Abbott Determine HIV-1/2 Whole Blood Assay (or other rapid test kit). Each kit contains 10 cards with 10 tests. The Chase Buffer (2.5 ml bottle) is supplied with the kit.
2. EDTA capillary tubes marked to indicate 50 µl, lancets, alcohol swabs and sterile gauze swabs. These are not supplied with the kit.

The kit needs to be stored at room temperature between 2 °C and 30 °C. Storage in a fridge is required during summer. The kit cannot be used after the expiry date.

B. The method of performing the HIV rapid test

1. Clean a fingertip with an alcohol swab and allow the finger to dry.
2. Remove a test strip from the foil cover.
3. Prick the skin of the fingertip with a lancet. Wipe the first drop of blood away with a sterile gauze swab.
4. Collect the next drop of blood with the EDTA tube. Either side of the tube can be used to collect blood. Fill the tube from the tip to the first black circle (i.e. 50 µl of blood). Avoid collecting air bubbles.
5. Apply the 50 µl of blood from the EDTA tube onto the sample pad marked with an arrow on the test strip.
6. Wait one minute until all the blood has been absorbed into the sample pad and then apply one drop of Chase Buffer. It is important that the bottle is held vertically (upside down) above the test strip when the drop of buffer is dropped onto the sample pad.

7. Wait a minimum of 15 minutes and then read the results. The maximum waiting time for reading the test is 20 minutes. After 20 minutes the test becomes invalid.

C. Reading the results of the HIV rapid test

1. **Positive**: A red bar will appear within both the Control window and the Patient window on the test strip. Any visible red bar in the Patient window must be regarded as positive. The result is positive even if the patient bar appears lighter or darker than the control bar.
2. **Negative**: A red bar will appear within the Control window and but no red bar is seen in the Patient window.
3. **Invalid**: If no red bar appears in the Control window, even if a red bar is visible in the Patient window. The result is invalid and the test must be repeated.

D. The interpretation of the HIV rapid test

The test is a specific test for HIV and will become positive when there are antibodies against HIV (the virus that cause AIDS) in the blood.

1. A positive test indicates that a person has antibodies against HIV. Therefore the person is infected with HIV.
2. A negative test indicates that a person does not have antibodies against HIV. Therefore the person is not infected with HIV, unless infected very recently and the HIV antibodies have not appeared yet.

E. Management if the HIV rapid test is positive

1. Explain to the patient that the first screening test for HIV is positive but that this should be confirmed with a second test.
2. Proceed with a second test using a kit from a different manufacturer.
3. If the second test is also positive, the patient is HIV positive.
4. Proceed with post-test counselling for a patient with a positive test.

F. Management if the first HIV rapid test is positive but the second is negative

1. A blood sample for an ELISA test must be sent to the laboratory.
2. The patient must be informed that the results of the HIV rapid tests are inconclusive and that a laboratory test is required to finally determine her HIV status.
3. If the ELISA test is positive the patient is HIV positive (i.e. HIV infected).
4. If the ELISA test is negative the patient is HIV negative (i.e. not HIV infected).
5. Proceed with appropriate counselling.